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L5 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2004:308529 Document No. 140:333599 Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening. Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi (Genox Research, Inc., Japan; Juntendo University). PCT Int. Appl. WO 2004031386 A1 20040415, 611 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9808 20030801. PRIORITY: JP 2002-229318 20020806; JP 2003-136543 20030514.
AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2004:162782 Document No. 140:216175 **Fc**.gamma.RIIB-specific antibodies and fragments for diagnosis and treatment of cancer, inflammation, autoimmune disease, allergy and immune disease. Koenig, Scott; Veri, Maria-Concetta (Macrogenics, Inc., USA). PCT Int. Appl. WO 2004016750 A2 20040226, 174 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK,

DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US25399 20030814. PRIORITY: US 2002-PV403266 20020814.

AB The present invention relates to antibodies or fragments thereof that specifically bind **Fc**.gamma.RIIB, particularly human **Fc** γRIIB, with greater affinity than said antibodies or fragments thereof bind **Fc**.gamma.RIIA, particularly human **Fc** γRIIA. The antibodies are humanized or chimeric derivs. of mouse monoclonal antibody 3H7 and 2B6. The invention provides methods of enhancing the therapeutic effect of therapeutic antibodies by administering the antibodies of the invention to enhance the effector function of the therapeutic antibodies. The invention also provides methods of enhancing efficacy of a vaccine composition by administering the antibodies of the invention.

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2003:355834 Document No. 138:362665 Immunostimulatory nucleic acids for the treatment of asthma and allergy. Bratzler, Robert L.; Petersen, Deanna M.; Fouron, Yves (USA). U.S. Pat. Appl. Publ. US 2003087848 A1 20030508, 221 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-776479 20010202. PRIORITY: US 2000-PV179991 20000203.

AB The invention involves administration of an immunostimulatory nucleic acid alone or in combination with an asthma/allergy medicament for the treatment or prevention of asthma and allergy in subjects. The combination of drugs are administered in synergistic amts. or in various dosages or at various time schedules. The invention also relates to kits and compns. concerning the combination of drugs.

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2002:977608 Document No. 138:54553 **Fc**.epsilon.-**Fc**.gamma. **fusion** proteins for treatment of allergy and asthma. An, Ling-Ling; Wu, Herren; Fung, Michael S. C. (Tanox, Inc., USA). PCT Int. Appl. WO 2002102320 A2 20021227, 33 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US19448 20020614. PRIORITY: US 2001-PV298710 20010615.

AB The present invention includes **Fc**.epsilon. fragments conjugated with **FC**.gamma. fragments, for example, **Fc** ε1-Hinge- **Fc**.epsilon.2-**Fc**.epsilon.3-**Fc** ε4- **Fc**.gamma.; Hinge-**Fc**.epsilon.2-**Fc** ε3- **Fc**.epsilon.4-**Fc**.gamma.; **Fc** ε2- **Fc**.epsilon.3-**Fc**.epsilon.4-**Fc** γ; **Fc**.epsilon.2-**Fc**.epsilon.3-**Fc** γ; **Fc**.epsilon.3-**Fc**.gamma.; and **Fc** ε3- **Fc**.epsilon.4-**Fc**.gamma., or any derivative or peptide, which has equivalent immunol. function. The **Fc**.gamma. fragment may be a fragment of any of the IgG subclasses (IgG1, IgG2, IgG3, or IgG4), preferably IgG1 or IgG3, wherein the fragment binds **Fc** γRIIB. The present invention also includes compns. suitable for administering to a patient suffering from an allergic disease comprising the **fusion** protein construct in a pharmaceutical composition including, for example, an excipient, diluant, or carrier. This treatment may be combined with anti-**IgE** therapy or allergen immunotherapy.

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2002:716299 Document No. 137:246549 Immunoglobulin **fusion** proteins that target low-affinity **Fc**.gamma. receptors. Arnason, Barry G. W.; Jensen, Mark A.; White, David M. (University of Chicago, USA). PCT Int. Appl. WO 2002072608 A2 20020919, 139 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US7365 20020311. PRIORITY: US 2001-PV274392 20010309.

AB The present invention concerns a family of nucleic acids, polypeptides and cloning vectors which direct expression of **fusion** proteins that can mimic aggregated IgG (AIG) and immune complex function with respect to their interactions with **Fc**.gamma.R and which allow for the inclusion and targeting of a second protein domain to cells expressing **Fc**.gamma.R. This was accomplished by expressing multiple linear copies of the hinge and CH2 domains (HCH2) of human IgG1 fused to the **Fc** region of human IgG1. Convenient restriction sites allow for the facile introduction of addnl. N-terminal domains. In one example, the extracellular domain of human CD8α was fused with 0-4 HCH2 segments and the **Fc** region of IgG1. The **fusion** protein was shown to stimulate proliferation of interleukin-2-primed natural killer cells.

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2002:409180 Document No. 137:1563 CD20/**IgE**-receptor like molecules and uses thereof. Welcher, Andrew A.; Calzone, Frank J. (USA). U.S. Pat. Appl. Publ. US 2002064823 A1 20020530, 46 pp., Cont.-in-part of U. S. Ser. No. 723,258. (English). CODEN: USXXCO. APPLICATION: US 2001-821821 20010329. PRIORITY: US 2000-PV193728 20000330; US 2000-723258 20001127.

AB Novel CD20/**IgE**-receptor like polypeptides and nucleic acid mols. encoding the same. The invention also provides vectors, host cells, agonists and antagonists (including selective binding agents), and methods for producing CD20/**IgE**-receptor like polypeptides. Also provided for are methods for the treatment, diagnosis, amelioration, or prevention of diseases with CD20/**IgE**-receptor like polypeptides.

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2001:149053 Document No. 134:206568 Polypeptide variants. Idusogie, Esohe Ekinaduese; Presta, Leonard G.; Mulkerrin, Michael George (Genentech, Inc., USA). U.S. US 6194551 B1 20010227, 30 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-282505 19990331. PRIORITY: US 1998-PV80447 19980402.

AB A variant of a polypeptide comprising a human **IgG Fc** region is described, which variant comprises an amino acid substitution at amino acid position 329, or at two or all of amino acid positions 329, 331 and 322 of the human **IgG Fc** region. Such variants display altered effector function. For example, C1q binding and/or complement dependent cytotoxicity (CDC) activity may be reduced or abolished in the variant polypeptide. The application also describes an immune complex and an assay for determining binding of an analyte, such as an **Fc** region-containing polypeptide, to a receptor.

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
2001:759124 Document No. 136:368335 Recombinant canine IL-13 receptor α2- **Fc fusion** protein inhibits canine allergen-specific-**IgE** production in vitro by peripheral blood mononuclear cells from allergic dogs. Tang, Liang; Boroughs, Karen L.; Morales, Tony; Stedman, Kim; Sellins, Karen; Clarke, Katie; McDermott, Martin; Yang, Shumin; McCall, Catherine (Heska Corporation, Fort Collins, CO, 80525, USA). Veterinary Immunology and Immunopathology, 83(1-2),

115-122 (English) 2001. CODEN: VIIMDS. ISSN: 0165-2427. Publisher: Elsevier Science B.V..

AB Human IL-13, like IL-4, is involved in the regulation of B-cell development, **IgE** synthesis and allergic responses. However, because IL-13 does not affect either murine Ig class switching or **IgE** production in vitro, the use of murine models to study the role of IL-13 in **IgE**-mediated diseases has been limited. In this communication, we report that recombinant protein of canine IL-13 (rcaIL-13) stimulates production of allergen-specific-**IgE** in vitro by peripheral blood mononuclear cells (PBMC) from flea allergen-sensitized dogs, and that this stimulation activity is specifically inhibited by recombinant protein of canine IL-13Rα2 and **Fc** fragment of canine IgG heavy chain (rcaIL-13Rα2- **Fc**). The data suggest that the regulatory effects of IL-13 on **IgE** production in canine PBMC are similar to those reported in humans. Thus, canine IL-13 may be a central mediator of allergic diseases in dogs, and allergic dogs may be excellent models for research on **IgE**-mediated diseases in humans.

L5 ANSWER 9 OF 12 MEDLINE on STN

1998269052. PubMed ID: 9604011. Evidence for involvement of two isoforms of Syk protein-tyrosine kinase in signal transduction through the high affinity **IgE** receptor on rat basophilic leukemia cells.
Yamashita T; Kairiyama L; Araki M; Nagasawa S. (Department of Hygienic Chemistry, Faculty of Pharmaceutical Sciences, Hokkaido University, Kita-ku, Sapporo, 060-0812, Japan.. yamashit@pharm.hokudai.ac.jp) . Journal of biochemistry, (1998 Jun) 123 (6) 1199-207. Journal code: 0376600. ISSN: 0021-924X. Pub. country: Japan. Language: English.

AB Recent evidence suggests a critical role for Syk in mast cell activation upon high affinity **IgE** receptor (FcepsilonRI) aggregation. A rat basophilic leukemia cell line, RBL-2H3, expresses similar levels of two Syk isoforms that differ with respect to the presence of a 23-amino acid insert within the "linker" region located between the second Src homology 2 and the catalytic domain. Although they exhibit comparable intrinsic enzymatic activity, functional differences between the two isoforms are unknown. Here we report that the deleted Syk isoform can mediate signal transduction in RBL-2H3 cells. Aggregation of chimeric kinase, consisting of either form of Syk fused to the transmembrane and extracellular domains of guinea pig type II **IgG Fc** receptor, on RBL transfectants resulted in degranulation, release of leukotrienes, and enhanced gene expression of tumor necrosis factor-alpha. The chimeras as well as phospholipase C-gamma1 and Vav became tyrosine-phosphorylated upon aggregation of chimeras. We also found that both Syk isoforms from transiently transfected COS-7 cells were capable of binding to phosphorylated FcepsilonRI, and their kinase activities were similarly up-regulated in the presence of tyrosine-phosphorylated synthetic peptides based on the sequence of the gamma subunit of FcepsilonRI. Thus, these results establish that both isoforms of Syk can mediate signal transduction in mast cells and suggest that the 23-amino acid insert in the linker region of Syk may not be obligatory for FcepsilonRI signaling.

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1998:692425 Document No. 130:94147 Chimeric anti-TAG72 receptors with immunoglobulin constant **Fc** domains and γ or ζ signalling chains. Hombach, Andreas; Sircar, Ranjan; Heuser, Claudia; Tillmann, Thorsten; Diehl, Volker; Kruis, Wolfgang; Pohl, Christoph; Abken, Hinrich (Klinik I fur Innere Medizin, Universitat zu Koln, Koln, D-50924, Germany). International Journal of Molecular Medicine, 2(1), 99-103 (English) 1998. CODEN: IJMMFG. ISSN: 1107-3756. Publisher: International Journal of Molecular Medicine.

AB The authors recently described the generation and expression of a chimeric T cell receptor with specificity for the tumor antigen TAG72 consisting of the single chain antibody (scFv) B72.3-scFv and the γ chain of the **Fc**.epsilon.RI receptor. The corresponding chimeric receptor

containing the ζ chain of the TCR as signaling unit is not functionally expressed reflecting that the requirements for functional expression of chimeric receptors containing the γ signaling chain are apparently different compared to those containing the CD3ζ signaling chain of the TCR. The authors describe a novel set of chimeric anti-TAG72 receptors including in their extracellular moiety the constant Ig CH2/3 domains that allow stable expression of chimeric γ as well as ζ receptors. The authors designed anti-TAG72 receptors that consist of a scFv fragment derived from an anti-TAG72 second generation antibody (CC49) and of the CH2/3 domains of the human IgG and intracellularly either of the ζ or γ signaling chain. The recombinant CC49-CH2/3-ζ and CC49-CH2/3-γ DNA, resp., was transfected into MD45 T cells and expressed under control of the RSV LTR. Both receptors were found on the cell membrane of transfected cells as demonstrated by flow cytometry anal. using an anti-human **IgG Fc** antibody directed to the CH2/3 Ig domains of the chimeric receptor. Specific crosslinking of the chimeric ζ as well as the γ receptor by antigen or anti-human Ig antibodies resulted in specific activation of transfected cells. The results demonstrate that both the γ chain and the ζ chain containing receptor are stably expressed and convert T cells to specificity for the TAG72 antigen. This receptor design will facilitate efficient generation of genetically modified peripheral T cells and may provide valuable tools for the cellular immunotherapy of TAG72+ tumors.

L5 ANSWER 11 OF 12 MEDLINE on STN

97435077. PubMed ID: 9291300. Challenge of BALB/c mice with respiratory syncytial virus does not enhance the Th2 pathway induced after immunization with a recombinant G **fusion** protein, BBG2NA, in aluminum hydroxide. Corvaia N; Tournier P; Nguyen T N; Haeuw J F; Power U F; Binz H; Andreoni C. (Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, France.) Journal of infectious diseases, (1997 Sep) 176 (3) 560-9. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB The polypeptide of aa 130-230 of the G protein (G2Na) of respiratory syncytial virus (RSV) was fused to BB, the albumin-binding region of streptococcal G protein, producing BBG2Na, which induced protective immune responses in rodent models. Evaluation of the immune response in mice immunized with BBG2Na in the adjuvant alhydrogel revealed high amounts of interleukin (IL)-5 and some IL-4 in splenocytes restimulated in vitro. This is compatible with a Th2 response. The activation of the Th2 pathway in such mice was further supported by the detection of IL-5 and G2Na-specific **IgE** in vivo. Of interest, in contrast to immunization with formalin-inactivated RSV, immunization of mice with BBG2Na followed by intranasal RSV challenge did not lead to increased production of IL-5- or G2Na-specific **IgE.** However, IgG1- and IgG2a-specific antibodies were boosted. These results demonstrate that the Th2 pathway is not enhanced by RSV challenge in BBG2Na-immunized mice.

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1993:619205 Document No. 119:219205 Plasmids for secretory expression of allergy-inhibition chimera protein of human in Escherichia coli. Kitai, Kazuo (Teijin Ltd, Japan). Jpn. Kokai Tokkyo Koho JP 05176772 A2 19930720 Heisei, 11 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1992-747 19920107.

AB The plasmids contain chimeric gene for human **IgE** and **IgG Fc** regions under the regulation of an alkalophilic Bacillus promoter and signal sequence were constructed for secretory expression in E. coli. PEG2 containing a synthetic sequence of human **IgE Fc** region and sequence for human **IgG Fc** region of pEXFC10 was constructed. The plasmid was transformed into Escherichia coli by known method. The recombinant E. coli produced the chimera protein and secreted the chimera protein in the culture supernatant.

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L2 6960 S L1 AND FC
L3 391 S L2 AND IGE
L4 12 S L3 AND IGG FC
L5 12 DUP REMOVE L4 (0 DUPLICATES REMOVED)

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L6 5 L3 AND MYELIN BASIC PROTEIN

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7 5 DUP REMOVE L6 (0 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
2004:308529 Document No. 140:333599 Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening. Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi (Genox Research, Inc., Japan; Juntendo University). PCT Int. Appl. WO 2004031386 A1 20040415, 611 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9808 20030801. PRIORITY: JP 2002-229318 20020806; JP 2003-136543 20030514.

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and **Fc**.epsilon.R binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-847208 20010501.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., **IgE**-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple

sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and **IgE** receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-847208 20010501; US 2001-439 20011024.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., **IgE**-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

2003:468095 Document No. 139:357756 Chimeric proteins: A novel approach for eliminating specific cell populations for targeted human therapy. Ben-Yehudah, Ahmi; Belostotsky, Ruth; Aqeilan, Rami; Azar, Yehudith; Steinberger, Ida; Fishman, Ala; Nechushtan, Amotz; Yarkoni, Shai; Lorberboum-Galski, Haya (Department of Cellular Biochemistry and Human Genetics, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel). Cellular and Molecular Mechanisms of Toxin Action, Volume 4, 148-167. Editor(s): Lazarovici, Philip. Taylor & Francis Ltd.: London, UK. (English) 2002. CODEN: 64JPAO.

AB A review. One of the most widely used toxins in chimeric proteins is the bacterial toxin Pseudomonas exotoxin (PE) produced by the bacterium Pseudomonas aeruginosa. Various chimeric proteins were constructed using two modified forms of the PE toxin: (a) in which Domain I is deleted, generating the PE40 truncated form of PE, (b) by introducing mutations into the binding domain (Domain I) of PE (at amino acid positions 57, 246, 247, 249, all substituted by Glu) to generate the PE664GOu mutated form of PE. The authors designed a number of chimeric proteins for the cure of unrelated disorders: autoimmune diseases, allergy and cancer. For each of these diseases the authors constructed chimeric proteins carrying a specific targeting moiety: Interleukin-2 (IL2) for eliminating activated T cells involved in many human diseases, **myelin basic protein** (MBP) for therapy of multiple sclerosis (MS), **Fc** ε for use in the treatment of asthma and other allergic disorders and gonadotropin releasing hormone (GnRH) for targeting adenocarcinomas.

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

1999:549393 Document No. 131:183867 Monovalent, multivalent, and multimeric

MHC binding domain **fusion** proteins and conjugates, and uses therefor. Wucherpfennig, Kai W.; Strominger, Jack L. (President and Fellows of Harvard College, USA). PCT Int. Appl. WO 9942597 A1 19990826, 113 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US3603 19990219. PRIORITY: US 1998-PV75351 19980219.

AB The present invention is directed to the design, production, and use of monovalent, multivalent and multimeric major histocompatibility complex binding domain **fusion** proteins and conjugates. The MHC **fusion** proteins and conjugates may comprise MHC class II α or β chain (HLA-DRA*0101, HLA-DRA*0102, HLA-DQA1*0301, HLA-DRB1*01, etc.), leucine zipper domain of Fos or Jun, linker peptide, yeast σ-mating factor secretion signal, human **myelin basic protein** tag, IgG or **IgE** or IgM **Fc**, and optionally cytotoxic substance (human desmoglein 3 protein peptide). The MHC binding domain **fusion** proteins and conjugates are useful for diagnosis and treatment of diseases associated with T cell-mediated immune response and antigen presentation, e.g. autoimmune disease, multiple sclerosis and rheumatoid arthritis. Thus, **fusion** proteins containing HLA-DR2 α chain (β chain), Fos (Jun) leucine zipper dimerization domain, VDGGGGG linker, and α-mating secretion signal were prepared, fused with IgG2a or IgM, tagged with MBP peptide, conjugated with bead carrier, and used for selectively depletion of T cells.

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PROCESSING COMPLETED FOR L3
L8          218 DUP REMOVE L3 (173 DUPLICATES REMOVED)

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L9            0 L8 AND "ANDREW SAXON"

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     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:58:12 ON
     29 OCT 2004
L1        639385 S FUSION
L2          6960 S L1 AND FC
L3           391 S L2 AND IGE
L4            12 S L3 AND IGG FC
L5            12 DUP REMOVE L4 (0 DUPLICATES REMOVED)
L6             5 S L3 AND MYELIN BASIC PROTEIN
L7             5 DUP REMOVE L6 (0 DUPLICATES REMOVED)
L8           218 DUP REMOVE L3 (173 DUPLICATES REMOVED)
L9             0 S L8 AND "ANDREW SAXON"

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L10           87 L1 AND IGE FC

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PROCESSING COMPLETED FOR L10
L11           51 DUP REMOVE L10 (36 DUPLICATES REMOVED)

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L11  ANSWER 1 OF 51  CAPLUS  COPYRIGHT 2004 ACS on STN
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2004:308529 Document No. 140:333599 Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening. Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi (Genox Research, Inc., Japan; Juntendo University). PCT Int. Appl. WO 2004031386 A1 20040415, 611 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9808 20030801. PRIORITY: JP 2002-229318 20020806; JP 2003-136543 20030514.

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

L11 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2004:162782 Document No. 140:216175 FcγRIIB-specific antibodies and fragments for diagnosis and treatment of cancer, inflammation, autoimmune disease, allergy and immune disease. Koenig, Scott; Veri, Maria-Concetta (Macrogenics, Inc., USA). PCT Int. Appl. WO 2004016750 A2 20040226, 174 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US25399 20030814. PRIORITY: US 2002-PV403266 20020814.

AB The present invention relates to antibodies or fragments thereof that specifically bind FcγRIIB, particularly human FcγRIIB, with greater affinity than said antibodies or fragments thereof bind FcγRIIA, particularly human FcγRIIA. The antibodies are humanized or chimeric derivs. of mouse monoclonal antibody 3H7 and 2B6. The invention provides methods of enhancing the therapeutic effect of therapeutic antibodies by administering the antibodies of the invention to enhance the effector function of the therapeutic antibodies. The invention also provides methods of enhancing efficacy of a vaccine composition by administering the antibodies of the invention.

L11 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2004:679170 Document No. 141:241999 Co-aggregation of FcγRII with FcεRI on Human Mast Cells Inhibits Antigen-induced Secretion and Involves SHIP-Grb2-Dok Complexes. Kepley, Christopher L.; Taghavi, Sharven; Mackay, Graham; Zhu, Daocheng; Morel, Penelope A.; Zhang, Ke; Ryan, John J.; Satin, Leslie S.; Zhang, Min; Pandolfi, Pier P.; Saxon, Andrew (Department of Internal Medicine, Virginia Commonwealth University Health Systems, Richmond, VA, 23298, USA). Journal of Biological Chemistry, 279(34), 35139-35149 (English) 2004. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Signaling through the high affinity IgE receptor FcεRI on human basophils and rodent mast cells is decreased by co-aggregating these receptors to the low affinity IgG receptor FcγRII. The authors used a recently described **fusion** protein, GE2, which is composed of

key portions of the human γ1 and the human ε heavy chains, to dissect the mechanisms that lead to human mast cell and basophil inhibition through co-aggregation of FcγRII and FcεRI. Unstimulated human mast cells derived from umbilical cord blood express the immunoreceptor tyrosine-based inhibitory motif-containing receptor FcγRII but not FcγRI or FcγRIII. Interaction of the mast cells with GE2 alone did not cause degranulation. Co-aggregating FcεRI and FcγRII with GE2 (1) significantly inhibited IgE-mediated histamine release, cytokine production, and Ca2+ mobilization, (2) reduced the antigen-induced morphol. changes associated with mast cell degranulation, (3) reduced the tyrosine phosphorylation of several cellular substrates, and (4) increased the tyrosine phosphorylation of the adapter protein downstream of kinase 1 (p62dok; Dok), growth factor receptor-bound protein 2 (Grb2), and SH2 domain containing inositol 5-phosphatase (SHIP). Tyrosine phosphorylation of Dok was associated with increased binding to Grb2. Surprisingly, in non-stimulated cells, there were complexes of phosphorylated SHIP-Grb2-Dok that were lost upon IgE receptor activation but retained under conditions of Fcε-Fcγ co-aggregation. Finally, studies using mast cells from Dok-1 knock-out mice showed that IgE alone triggers degranulation supporting an inhibitory role for Dok degranulation. The authors' results demonstrate how human FcεRI-mediated responses can be inhibited by co-aggregation with FcγRIIB and implicate Dok, SHIP, and Grb2 as key intermediates in regulating antigen-induced mediator release.

L11 ANSWER 4 OF 51 MEDLINE on STN DUPLICATE 1
2004433011. PubMed ID: 15316510. Inhibition of allergen-specific IgE reactivity by a human Ig Fcgamma-Fcepsilon bifunctional **fusion** protein. Zhang Ke; Kepley Christopher L; Terada Tetsuya; Zhu Daocheng; Perez Hector; Saxon Andrew. (Hart and Louis Lyon Laboratory, Division of Clinical Immunology and Allergy, Department of Medicine, University of California Los Angeles School of Medicine, CA 90095-1680, USA.) Journal of allergy and clinical immunology, (2004 Aug) 114 (2) 321-7. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Coaggregating FcepsilonRI with FcgammaRII receptors holds great potential for treatment of IgE-mediated disease by inhibiting FcepsilonRI signaling. We have previously shown that an Fcgamma-Fcepsilon **fusion** protein, human IgG-**IgE Fc** **fusion** protein (GE2), could inhibit FcepsilonRI-mediated mediator releases in vitro and in vivo. OBJECTIVE: We sought to test whether GE2 was capable of blocking mediator release from FcepsilonRI cells sensitized with IgE in vivo or in vitro before exposure to GE2, a critical feature for GE2 to be clinically applicable. METHODS: GE2 was tested for its ability to inhibit Fel d 1-induced mediator release from human blood basophils from subjects with cat allergy, human lung-derived mast cells, human FcepsilonRIalpha transgenic mice sensitized with human cat allergic serum, and rhesus monkeys naturally allergic to the dust mite Dermatophagoides farinae. RESULTS: Basophils from subjects with cat allergy and lung mast cells degranulate when challenged with Fel d 1 and anti-IgE, respectively. GE2 itself did not induce mediator release but strongly blocked this Fel d 1- and anti-IgE-driven mediator release. GE2 was able to block Fel d 1-driven passive cutaneous anaphylaxis at skin sites sensitized with human serum from subjects with cat allergy in human FcepsilonRIalpha transgenic mice, but by itself, GE2 did not induce a passive cutaneous anaphylaxis reaction. Finally, GE2 markedly inhibited skin test reactivity to D farinae in monkeys naturally allergic to this allergen, with complete inhibition being observed at 125 ng. CONCLUSION: GE2 is able to successfully compete for FcepsilonRs and FcgammaRs on cells presensitized in vitro and in vivo and lead to inhibition of IgE-mediated reactivity through coaggregation of FcepsilonRI with FcgammaRII.

L11 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
2004:109284 Document No. 140:269419 Utilizing Fcε-Bak chimeric protein for studying **IgE-Fc**.epsilon.RI interactions.

Belostotsky, Ruth; Lorberboum-Galski, Haya (Hadassah Medical School, Department of Cellular Biochemistry and Human Genetics, Hebrew University, Jerusalem, 91120, Israel). Clinical Immunology (San Diego, CA, United States), 110(1), 89-99 (English) 2004. CODEN: CLIIFY. ISSN: 1521-6616. Publisher: Elsevier Science.

AB The authors previously constructed a pro-apoptotic Fcε-Bak chimeric protein, targeted against cells expressing the IgE high affinity receptor (FcεRI). The authors demonstrated that the chimeric protein is internalized by target mast cells and kills them. These results, which constitute a promising basis for applying this approach to antiallergic therapy, raise some theor. questions with respect to two major issues: (a) is the monomeric Fcε-Bak-FcεRI complex able to undergo endocytosis, and (b) does the receptor binding domain of human **IgE** (**Fc**.epsilon.) react with rodent FcεRI. In an attempt to answer these questions, the authors have now thoroughly investigate the interaction of human (h) and mouse (m) Fcε-Bak with FcεRI-pos. cells. Using established cultures of rodent and human origin, as well as a primary mouse mast cell culture, the authors demonstrate that binding of the chimeric protein to the membrane is followed by quick endocytosis, leading to the apoptosis of specific cells. The authors also confirm that this interaction depends on FcεRI and not on other IgE receptors. The authors found that the effect of Fcε-Bak on the cells depends on the level of surface FcεRI expression, but not on the origin of the target cells or of the Fcε moiety. The authors suggest that endocytosis of the monomeric Fcε-Bak-FcεRI complex results from the inability of Fcε-Bak to transduce signals, characteristic of the monomeric **IgE-Fc**.epsilon.RI complex due to the absence of the variable portion of the IgE mol. The results also indicate that at least the Fcε fragment of human IgE is able to interact with both human and rodent FcεRI.

L11 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-847208 20010501.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L11 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2003:241912 Document No. 138:265639 Inhibiting the degranulation in mastocytes using a hybrid protein comprising a receptor-binding protein fused to a protease cleaving a protein of the secretion process. Bigalke, Hans; Frevert, Jurgen (Biotecon Gesellschaft Fur Biotechnologische Entwicklung Und Consulting Mbh, Germany). U.S. Pat. Appl. Publ. US 2003059912 A1 20030327, 7 pp., Cont.-in-part of U.S. Ser. No. 700,540. (English). CODEN: USXXCO. APPLICATION: US 2002-64903 20020827. PRIORITY: DE 1998-19821285 19980513; WO 1999-EP3272 19990512; US 2001-700540 20010119.

AB A hybrid protein is provided containing a protein that binds to a receptor of mastocytes and basophils and is endocytosed by them. The protein can be IgE, IgE fragment, **IgE Fc** fragment, antibody against the IgE receptor of mastocytes and basophils, a fragment of the antibody against the IgE receptor of mastocytes and basophils, an antibody against mastocyte-specific potassium channel, or mast cell degranulating peptide. The hybrid protein also contains a protease which cleaves proteins of the secretion process of the mastocytes and basophils so as to inhibit the secretion process without killing the mastocytes and basophils. The protease can be the light chain of Clostridium botulinum toxin or its proteolytic fragments containing a His-Xaa-Xaa-Xaa-His-Xaa-Xaa-His sequence, the light chain of the tetanus toxin or proteolytically active fragment of the light chain containing His-Asp-Leu-Ile-His-Val-Leu-His, or an IgA protease of Neisseria gonorrhoeae and its proteolytic domain. Thus, a hybrid protein comprising IgE fused to the light chain of either Clostridium botulinum toxin or tetanus toxin prevents allergic shock caused by dying mastocytes.

L11 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
2003:621944 Document No. 139:291008 FcεRI-FcγRII Coaggregation inhibits IL-16 production from human Langerhans-like dendritic cells. Kepley, Christopher L.; Zhang, Ke; Zhu, Daocheng; Saxon, Andrew (Medical College of Virginia, Department of Internal Medicine, Virginia Commonwealth University, Richmond, VA, USA). Clinical Immunology (San Diego, CA, United States), 108(2), 89-94 (English) 2003. CODEN: CLIIFY. ISSN: 1521-6616. Publisher: Elsevier Science.
AB Langerhans-like dendritic cells (LLDC) express the high-affinity IgE receptor FcεRI form that lacks the β-chain, and may play an important role in allergic inflammation via production of IL-16. Secretion of mediators by human mast cells and basophils is mediated via FcεRI and is decreased by coaggregating these receptors to the low-affinity IgG receptor, FcγRII. The authors used a recently described human Ig **fusion** protein (GE2), which is composed of key portions of the human γ1 and the human ε heavy chains, to investigate its ability to inhibit IL-16 production from FcεRI-pos. Langerhans-like dendritic cells through coaggregation of FcγRII and FcεRI. Unstimulated LLDC-derived from CD14-pos. monocytes from atopic donors were shown to express FcγRII, an ITIM-containing receptor, but not FcεRI or FcγRIII which are activating (ITAM) receptors. When passively sensitized with antigen-specific, human IgE and then challenged with antigen, LLDC were stimulated to produce IL-16. However, when FcεRI and FcγRII were coaggregated with GE2, IL-16 production was inhibited. Exposure of LLDCs to GE2 alone did not induce IL-16 production The authors' results further extend their studies demonstrating the ability of GE2 to inhibit FcεRI-mediated responses via coaggregation with FcγRIIB and at the same time show that human LDCC can be modulated in a fashion similar to mast cells and basophils.

L11 ANSWER 9 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
2003088063 EMBASE Human FcεRIα-specific human single-chain Fv (scFv) antibody with antagonistic activity toward **IgE/Fc** εRIα-binding. Hashiguchi S.; Nakashima T.; Nitani A.; Yoshihara T.; Yoshinaga K.; Ito Y.; Maeda Y.; Sugimura K.. K. Sugimura, Department of Bioengineering, Faculty of Engineering, Kagoshima University, 1-21-40 Korimoto, Kagoshima 890-0065, Japan. kazu@be.kagoshima-u.ac.jp. Journal of Biochemistry 133/1 (43-49) 1 Jan 2003.
Refs: 32.
ISSN: 0021-924X. CODEN: JOBIAO. Pub. Country: Japan. Language: English. Summary Language: English.
AB The α-chain of FcεRI (FcεRIα) plays a critical role in the binding of IgE to FcεRI. A fully human antibody interfering with this interaction may be useful for the prevention of IgE-mediated allergic diseases. Here, we describe the successful isolation

of a human single-chain Fv antibody specific to human FcεRIα using human antibody phage display libraries. Using the non-immune phage antibody libraries constructed from peripheral blood lymphocyte cDNA from 20 healthy subjects, we isolated three phage clones (designated as FcRε27, FcRε51, and FcRε70) through two rounds of bio-panning selection. The purified soluble scFv, FcRε51, inhibited the binding of IgE to recombinant FcεRIα, although both FcRε27 and FcRε70 showed fine binding specificity to FcεRIα. Since FcRε51 was determined to be a monomer by HPLC, BIAcore analysis was performed. The dissociation constant of FcRε51 to FcεRIα was estimated to be 20 nM, i.e., fortyfold lower than that of IgE binding to FcεRIα (K(d) = 0.5 nM). With these characteristics, FcRε51 exhibited inhibitory activity on the release of histamine from passively sensitized human peripheral blood mononuclear cells.

L11 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
2002:977608 Document No. 138:54553 Fcε-Fcγ **fusion** proteins for treatment of allergy and asthma. An, Ling-Ling; Wu, Herren; Fung, Michael S. C. (Tanox, Inc., USA). PCT Int. Appl. WO 2002102320 A2 20021227, 33 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US19448 20020614. PRIORITY: US 2001-PV298710 20010615.

AB The present invention includes Fcε fragments conjugated with FCγ fragments, for example, Fcε1-Hinge-Fcε2-Fcε3-Fcε4-Fcγ; Hinge-Fcε2-Fcε3-Fcε4-Fcγ; Fcε2-Fcε3-Fcε4-Fcγ; Fcε2-Fcε3-Fcγ; Fcε3-Fcγ; and Fcε3-Fcε4-Fcγ, or any derivative or peptide, which has equivalent immunol. function. The Fcγ fragment may be a fragment of any of the IgG subclasses (IgG1, IgG2, IgG3, or IgG4), preferably IgG1 or IgG3, wherein the fragment binds FcγRIIB. The present invention also includes compns. suitable for administering to a patient suffering from an allergic disease comprising the **fusion** protein construct in a pharmaceutical composition including, for example, an excipient, diluant, or carrier. This treatment may be combined with anti-IgE therapy or allergen immunotherapy.

L11 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-847208 20010501; US 2001-439 20011024.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e.,

IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L11 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2002:449715 Document No. 137:28591 Preparation of GLP-1 **fusion** proteins for use in treating diabetes mellitus and other conditions. Glaesner, Wolfgang; Micanovic, Radmilla; Tschang, Sheng-Hung Rainbow (Eli Lilly and Company, USA). PCT Int. Appl. WO 2002046227 A2 20020613, 200 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US43165 20011129. PRIORITY: US 2000-PV251954 20001207.

AB The present invention relates to glucagon-like peptide-1 compds. fused to proteins that have the effect of extending the in vivo half-life of the peptides. The heterologous **fusion** proteins of the invention comprise a GLP-1 compound fused to human albumin, a human albumin analog or fragment, the Fc portion of an Ig, or an analog or fragment of the Fc portion of an Ig. These **fusion** proteins can be used to treat non-insulin dependent diabetes mellitus as well as a variety of other conditions. Pharmaceutical formulations containing the **fusion** proteins and polynucleotides encoding the proteins are also claimed.

L11 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2002:925313 Document No. 138:23638 Non-anaphylactogenic constant region fragments of IgE for vaccines. Brown, Tracy Michelle; Morsey, Mohammed Ali (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1262491 A2 20021204, 50 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2002-253606 20020522. PRIORITY: US 2001-PV292638 20010522.

AB The authors disclose the use of antigenic peptides derived from the Fc portion of the ε heavy chain of IgE from two unrelated species as vaccines for the treatment and prevention of IgE-mediated allergic disorders.

L11 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

2002:15409 Document No. 136:197386 Utilizing Chimeric Proteins for Exploring the Cellular Fate of Endogenous Proteins. Ben-Yehudah, Ahmi; Aqeilan, Rami; Belostotsky, Ruth; Azar, Yehudith; Lorberboum-Galski, Haya (Department of Cellular Biochemistry and Human Genetics, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel). Biochemical and Biophysical Research Communications, 290(1), 332-338 (English) 2002. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Academic Press.

AB We recently designed and constructed chimeric proteins for the elimination of specific cell populations. These chimeric proteins are composed of a targeting component fused to an apoptotic protein as the killing moiety. However, chimeric proteins can serve not only to eliminate cell populations, but also as "biol. tools" for studying the fate of endogenous

proteins. We show here that upon entering their target cell, a variety of chimeric proteins composed of an endogenous protein as their killing moiety reach the subcellular location of their endogenous counterpart. In contrast, bacterial-based killing domains head for the subcellular site of their substrate. Moreover, the chimeric protein acts similarly to the endogenous protein, while causing the cell to die. Therefore, chimeric proteins may serve as a unique tool for investigating cellular proteins and their intracellular localization, without the need to overexpress them. (c) 2002 Academic Press.

L11 ANSWER 15 OF 51 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2001:373343 The Genuine Article (R) Number: 428WV. Targeting dendritic cells to enhance DNA vaccine potency. You Z Y; Huang X; Hester J; Toh H C; Chen S Y (Reprint). Baylor Coll Med, Ctr Cell & Gene Therapy, Alkek Bldg, N1004, 1 Baylor Pl, Houston, TX 77030 USA (Reprint); Baylor Coll Med, Ctr Cell & Gene Therapy, Houston, TX 77030 USA; Baylor Coll Med, Dept Mol & Human Genet, Houston, TX 77030 USA; Baylor Coll Med, Dept Pediat, Houston, TX 77030 USA. CANCER RESEARCH (1 MAY 2001) Vol. 61, No. 9, pp. 3704-3711. Publisher: AMER ASSOC CANCER RESEARCH. PO BOX 11806, BIRMINGHAM, AL 35202 USA. ISSN: 0008-5472. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB DNA vaccination that can induce both cellular and humoral immune responses has become an attractive immunization strategy against cancer and infection. Dendritic cells (DCs) play a critical role in the induction of immune responses by DNA vaccination. However, a major problem of DNA vaccination is its limited potency, because only a very limited fraction of injected DNA molecules are taken up by DCs. In this study, we describe a novel DNA vaccination strategy to enhance uptake and presentation of antigens by DCs. Specifically, we developed a DNA vaccine based upon expression of a model hepatitis B virus (HBV) e antigen fused to an **Ige Fc** fragment. After vaccination, the DNA are taken up hy cells that produce and secrete the antigen-Fc **fusion** proteins. The secreted **fusion** proteins, in addition to inducing B cells, are efficiently captured and processed by DCs via receptor-mediated endocytosis and then presented to the MHC class II and as -I (cross-priming). The results of this study demonstrate that broad enhancement of antigen-specific CD4+ helper, CD8+ cytotoxic T-cell, and B-cell responses can be achieved by this DNA vaccination strategy, Thus, the strategy capable of inducing all arms of the adaptive immunity may provide a novel, generic design for the development of therapeutic and preventive DNA vaccines.

L11 ANSWER 16 OF 51 MEDLINE on STN

2001423280. PubMed ID: 11325715. Cross-correlation analysis of inner-leaflet-anchored green fluorescent protein co-redistributed with IgE receptors and outer leaflet lipid raft components. Pyenta P S; Holowka D; Baird B. (Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca, New York 14853, USA.) Biophysical journal, (2001 May) 80 (5) 2120-32. Journal code: 0370626. ISSN: 0006-3495. Pub. country: United States. Language: English.

AB To investigate the structural basis for membrane interactions that occur between Lyn tyrosine kinase and **IgE-Fc**(epsilon)RI or other components of lipid rafts, we prepared a green fluorescent protein analog of Lyn (PM-EGFP) and used cross-correlation analysis to quantify co-redistributions of aggregates that occur after **IgE-Fc** (epsilon)RI is cross-linked on the cell surface. PM-EGFP, which contains minimally the palmitoylation and myristoylation sites on Lyn, was compared with another inner leaflet probe, EGFP-GG, which contains a prenylation site and a polybasic sequence similar to K-ras. Confocal fluorescence microscopy was used to examine co-redistributions of these inner leaflet components with **IgE-Fc**(epsilon)RI and outer leaflet raft components, ganglioside GD1b and glycosylphosphotidylinositol-linked Thy-1, under conditions where the latter were cross-linked externally to form large patches at the cell surface. The cross-correlation analysis

was developed and characterized with simulations representing cell surface distributions, and parameters from the cross-correlation curves, rho(o) (peak height) and A (peak area), were shown to be reliable measures of the extent of co-redistributed aggregates and their size. Cross-correlation analysis was then applied to quantify co-redistributions of the fluorescently labeled inner and outer leaflet components on RBL-2H3 cells. As visually observed and parameterized in this manner, PM-EGFP was found to co-redistribute with lipid rafts significantly more than EGFP-GG or an endogenous prenylated protein, Cdc42. These quantitative results are consistent with previous analyses of Lyn co-redistributions and support the hypothesis that the functionally important interaction of Lyn with cross-linked **IgE**- **Fc**(epsilon)RI is due to their mutual co-association with lipid rafts.

L11 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
2001:26277 Document No. 134:206467 Redirecting mouse CTL against colon carcinoma: superior signaling efficacy of single-chain variable domain chimeras containing TCR-ζ vs FcεRI-γ. Haynes, Nicole M.; Snook, Marie B.; Trapani, Joseph A.; Cerruti, Loretta; Jane, Stephen M.; Smyth, Mark J.; Darcy, Phillip K. (Cancer Immunology, Peter MacCallum Cancer Institute, Victoria, 8006, Australia). Journal of Immunology, 166(1), 182-187 (English) 2001. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.
AB The structurally related TCR-ζ and Fc receptor for **IgE** (**Fc**.epsilon.RI)-γ are critical signaling components of the TCR and FcεRI, resp. Although chimeric Ab receptors containing ζ and γ signaling chains have been used to redirect CTL to tumors, a direct comparison of their relative efficacy has not previously been undertaken. Here, in naive T lymphocytes, we compare the signaling capacities of the ζ and γ subunits within single-chain variable domain (scFv) chimeric receptors recognizing the carcinoembryonic Ag (CEA). Using a very efficient retroviral gene delivery system, high and equivalent levels of scFv-ζ and scFv-γ receptors were expressed in T cells. Despite similar levels of expression and Ag-specific binding to colon carcinoma target cells, ligation of scFv-anti-CEA-ζ chimeric receptors on T cells resulted in greater cytokine production and direct cytotoxicity than activation via scFv-anti-CEA-γ receptors. T cells expressing scFv-ζ chimeric receptors had a greater capacity to control the growth of human colon carcinoma in scid/scid mice or mouse colon adenocarcinoma in syngeneic C57BL/6 mice. Overall, these data are the first to directly compare and definitively demonstrate the enhanced potency of T cells activated via the ζ signaling pathway.

L11 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
1999:764208 Document No. 132:10492 Chimeric molecules comprising an extracellular ligand-binding domain of a receptor and an **IgE** **Fc** or constant region, and their use in assay systems. Stahl, Neil; Karow, Margaret; Yancopoulos, George D. (Regeneron Pharmaceuticals, Inc., USA; The Procter & Gamble Co.). PCT Int. Appl. WO 9961630 A2 19991202, 55 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US11619 19990526. PRIORITY: US 1998-84697 19980526.
AB The present invention provides for a general, rapid, cell-based assay system that utilizes the unique features of the IgE high affinity receptor FcεRI and the rapid, characteristic degranulation phenotype exhibited by mast cells and basophils following antigen binding to, and crosslinking of, monomeric IgE bound to the receptor on such cells. Identifying a ligand for a receptor comprises contacting a cell expressing a cell surface FcεRI with a chimeric polypeptide comprising an

extracellular ligand-binding domain of a receptor and an IgE constant or Fc region, and and detecting or measuring ligand binding to the complex. The invention further provides for chimeric polypeptide mols., the nucleic acids encoding the chimeric polypeptide mols., and cell lines expressing the chimeric polypeptide mols. In particular, the chimeric polypeptide mols. comprise an extracellular ligand binding domain selected from the granulocyte colony-stimulating factor receptor, the muscle-specific kinase receptor, the bone morphogenic protein receptor, the leptin receptor, the ciliary neurotrophic factor receptor α, the gp130 receptor, and the erythropoietin receptor.

L11 ANSWER 19 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2

1999018652 EMBASE Polyethylene glycol-mediated infection of non-permissive mammalian cells with semliki forest virus: Application to signal transduction studies. Arudchandran R.; Brown M.J.; Song J.S.; Wank S.A.; Haleem-Smith H.; Rivera J.. J. Rivera, Building 10, MSC 1820, 10 Center Drive, Bethesda, MD 20892-1820, United States. Journal of Immunological Methods 222/1-2 (197-208) 1999.
Refs: 24.
ISSN: 0022-1759. CODEN: JIMMBG.
Publisher Ident.: S 0022-1759(98)00161-6. Pub. Country: Netherlands.
Language: English. Summary Language: English.

AB Semliki Forest Virus (SFV) vectors allow the subcloning of a gene of interest directly in the expression vector, thus avoiding the need to select and purify viral recombinants, making this viral expression system attractive over many others for mammalian protein expression. We now describe a novel and generally applicable method for infection of non-permissive mammalian cells with SFV, that greatly enhances the utility of this expression system. We demonstrate that the hygroscopic polymer poly (ethylene glycol), PEG, promotes the infectivity of cells by SFV under conditions that did not promote cell-cell **fusion.** We also found that the PEG-induced infection and expression of an exogenous protein (green fluorescent protein, GFP) did not elevate the basal tyrosine kinase activity, induce a stress-activated responses, or result in aberrant cell responses. Expression of GFP tagged- Vav, an activator of stress-activated protein kinase (SAPK/JNK), resulted in the expected induction of JNK activity and in the normal redistribution of Vav in response to engagement of the high affinity receptor for **IgE** (**Fc**.epsilon.RI). Thus, our findings that PEG allows the infection of non-permissive cells by SFV makes this system extremely attractive for expression of proteins in mammalian cells, and studies on signal transduction and cellular localization in immune and non-immune cells.

L11 ANSWER 20 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1998:394352 Document No. 129:49650 Inhibition of IgE-mediated allergies by a human IgE-derived oligopeptide. Padlan, Eduardo A.; Birgit, A. Helm (United States Dept. of Health and Human Services, USA; Padlan, Eduardo A.; Birgit, A. Helm). PCT Int. Appl. WO 9824808 A2 19980611, 45 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US22348 19971205. PRIORITY: US 1996-31991 19961206.

AB Peptides are disclosed that are capable of effective recognition of the human **IgE Fc**.epsilon. receptor. The peptides partially comprise a fragment of human IgE. By addition of constraining amino acid residues at or near the polypeptides' N- and C-termini, these peptides may be forced to assume a loop configuration. These constrained peptides are useful as competitors of human IgE for the Fcε receptor, and may be used to block the development of type I hypersensitivity. Oligopeptide CLSRPSPFDLFIRKSPTITSCC was incubated in 50

mM ammonium bicarbonate to form the constrained peptide. Antisera to the peptide were raised in rabbits. The antisera inhibited IgE binding to receptor.

L11 ANSWER 21 OF 51 MEDLINE on STN DUPLICATE 3
1999077535. PubMed ID: 9862699. Production of a chimeric form of CD23 that is oligomeric and blocks IgE binding to the Fc epsilonRI. Kelly A E; Chen B H; Woodward E C; Conrad D H. (Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond 23298, USA.) Journal of immunology (Baltimore, Md. : 1950), (1998 Dec 15) 161 (12) 6696-704. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The low affinity receptor for **IgE** (**Fc** epsilonRII/CD23) has previously been shown to interact with IgE with a dual affinity. Three chimeric constructs were created containing the lectin domain (amino acids 172-188) or the "neck" and lectin domain (amino acids 157-188) attached to subunits of oligomeric proteins. All chimeras were incapable of interacting with IgE with either a high or low affinity, indicating that the alpha-helical stalk of CD23 is important for orienting the lectin heads such that an interaction with IgE can occur. This concept received further support in that a chimeric CD23 composed of the human CD23 stalk and the mouse CD23 lectin head bound mouse IgE with a dual affinity, but could only bind rat IgE with a low affinity. Effort was next concentrated on a construct consisting of the entire extracellular (EC) region of CD23. A mutation to the first cleavage site of CD23 (C1M) resulted in a more stable molecule as determined by a decrease of soluble CD23 release. A soluble chimeric EC-C1M was prepared by attaching an isoleucine zipper to the amino terminus (lzEC-C1M). The interaction with IgE by lzEC-C1M was found to be superior to that seen with EC-CD23. The lzEC-C1M could inhibit binding of IgE to both CD23 and the high affinity receptor for **IgE**, **Fc** epsilonRI, providing further evidence for a strong interaction with IgE. Fc epsilonRI inhibition (approximately 70%) was seen at equimolar concentrations of lzEC-C1M, implying the effectiveness of this chimera and suggesting its potential therapeutic value.

L11 ANSWER 22 OF 51 MEDLINE on STN
1999008539. PubMed ID: 9794408. Fc epsilonRI-mediated induction of TNF-alpha gene expression in the RBL-2H3 mast cell line: regulation by a novel NF-kappaB-like nuclear binding complex. Pelletier C; Varin-Blank N; Rivera J; Iannascoli B; Marchand F; David B; Weyer A; Blank U. (Unite Immuno-Allergie, Institut Pasteur, Paris, France.) Journal of immunology (Baltimore, Md. : 1950), (1998 Nov 1) 161 (9) 4768-76. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Using rat basophilic leukemia (RBL-2H3) cells as a model, we investigated how aggregation of the high affinity receptor for **IgE** (**Fc** epsilonRI) regulates TNF-alpha gene expression. Antigenic stimulation of RBL-2H3 cells led to an increase in newly synthesized TNF-alpha mRNA that was dependent on continuous receptor aggregation and did not require de novo protein synthesis. Kinetic analysis showed that maximal levels were achieved at 60 min and waned by 180 min of stimulation. Concomitant with the transcriptional activation of the TNF-alpha gene, the rapid appearance and disappearance of a previously uncharacterized nuclear NF-kappaB DNA binding activity, comprised of two distinct protein complexes, were observed. These protein complexes bound to NF-kappaB sites within the TNF-alpha gene and contained novel proteins (three species of Mr between 90,000-110,000) distinct from the classical proteins in NF-kappaB complexes. The induced NF-kappaB binding activity required continuous receptor stimulation and induced NF-kappaB-dependent reporter gene expression. Consistent with a role for the novel NF-kappaB nuclear binding activity in TNF-alpha gene expression, deletion of several 5' kappaB elements in the TNF-alpha promoter abolished all measurable Fc epsilonRI-dependent induction of a reporter construct. Pharmacologic agents that inhibited the NF-kappaB binding activity also inhibited TNF-alpha mRNA expression. Our results demonstrate that a novel

NF-kappaB-like nuclear binding activity plays an important role in regulation of the rapid and transient transcriptional activation of the TNF-alpha gene via Fc epsilonRI.

L11 ANSWER 23 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 4

1999021388 EMBASE The membrane-proximal part of FcεRIα contributes to human IgE and antibody binding - Implications for a general structural motif in Fc receptors. Nechansky A.; Aschauer H.; Kricek F.. F. Kricek, Novartis Forschungsinstitut GmbH, Brunnerstrasse 59, 1230 Vienna, Austria. franz.kricek@pharma.novartis.com. FEBS Letters 441/2 (225-230) 1998.

Refs: 25.

ISSN: 0014-5793. CODEN: FEBLAL.

Publisher Ident.: S 0014-5793(98)01558-0. Pub. Country: Netherlands.

Language: English. Summary Language: English.

AB The high affinity receptor for human **IgE** (**Fc** εRI) on tissue mast cells and blood basophils is responsible for immediate hypersensitivity reactions. Binding of human IgE (hIgE) to FcεRI has been shown to be mediated via three independent regions in the extracellular part of the α-subunit of FcεRI (ecFcεRIα). By site-directed mutagenesis we investigated the contribution of amino acids within the ecFcεRIα FG loop (residues Lys154-Leu165) to binding to hIgE and two monoclonal anti-FcεRIα antibodies (15/1, 5H5/F8). The mutated receptors were expressed and secreted from eukaryotic cells as amino-terminal **fusion** to HSA. We show that the proposed loop region contributes partly to hIgE binding and that the epitope of mAb 15/1, which inhibits hIgE/FcεRIα interaction, maps to this region whereby a single W156A mutation results in complete loss of mAb 15/1 binding. In contrast, hIgE binding is not affected by the W156A mutation indicating that different amino acid residues within the loop are recognized by the mAbs 15/1 and hIgE. MAb 5H5/F8 does not recognize a receptor mutant truncated to Ile170. By screening a random dodecapeptide library displayed on bacterial flagella the epitope for mAb 5H5/F8 was mapped to P173REKY177 whereas one of the 15/1 binding clones displayed a peptide with an amino acid sequence homologous to Leu158-Ile167. Based on the epitopes identified for the inhibitory mAb 15/1 and the non-inhibitory mAb 5H5F8 and on binding data obtained with polyclonal antisera raised against two ecFcεRIα peptides, we propose a structural element in the membrane proximal part of ecFcεRIα which forms a 3D structure which might facilitate specific and efficient attachment of hIgE. Copyright (C) 1998 Federation of European Biochemical Societies.

L11 ANSWER 24 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1998:425049 Document No. 129:215641 Chimeric scFv/γ receptor-mediated T-cell lysis of tumor cells is coregulated by adhesion and accessory molecules. Weijtens, M. E. M.; Willemsen, R. A.; Van Krimpen, B. A.; Bolhuis, R. L. H. (Department of Clinical and Tumor Immunology, Daniel den Hoed Cancer Center, Rotterdam, Neth.). International Journal of Cancer, 77(2), 181-187 (English) 1998. CODEN: IJCNAW. ISSN: 0020-7136. Publisher: Wiley-Liss, Inc..

AB Adhesion and accessory mols. play a critical role in T-cell activation and effector function in general and in tumor cell recognition and lysis in particular. We investigated the contribution of CD2, CD3, CD11a/CD18, CD54 and CD58 mols. in T lymphocyte-tumor cell interactions mediated by chimeric Ig receptors. The chimeric receptor is composed of a single chain antibody binding site and a γ-chain signal transducing mol. (scFv/γ). T lymphocytes expressing such scFv/γ receptors recognize the G250 Ag on renal cell carcinoma (RCC) in an major histocompatibility complex (MHC)-unrestricted manner and exert RCC selective cytolysis. A coregulatory role for CD2, CD3 and CD11a/CD18 mols. in scFv/γ-mediated cytolysis was demonstrated using monoclonal antibody (MAb)-induced inhibition of scFv/γ-mediated cytolysis. The inhibition of lysis was not due to inhibition of cytotoxic T lymphocyte

(CTL)-target cell conjugation but rather to a post-conjugate signaling event. Binding of CD54 and CD58 MAbs to the RCC did not inhibit cytolysis of RCC cells that expressed high levels of both CD54 and the G250 antigen (Ag) (A75), whereas cytolysis of RCC expressing intermediate levels of CD54 and G250 Ag (SK-RC-17 cl.4) was partly inhibited by the CD54 MAb. Binding of low concns. of G250 MAb to RCC (A75) rendered these cells sensitive to CD54 MAb inhibition, demonstrating a direct functional relation between G250 Ag expression level and adhesion mols. Taken together, our findings indicate a coregulatory role for CD2, CD3 and CD11a/CD18 mols. in the scFv/γ-mediated cytolysis of tumor cells and show that the requirement of CD11a/CD18-CD54 interactions is dependent on the level of free Ag. This makes these gene-transduced T lymphocytes attractive tools for adoptive immunogene therapy of cancer.

L11 ANSWER 25 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1997:713250 Document No. 128:21611 Interaction of human IgE with soluble forms of IgE high affinity receptors. Liu, Jun; Ruppel, Jane; Shire, Steven J. (Department of Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, CA, 94080, USA). Pharmaceutical Research, 14(10), 1388-1393 (English) 1997. CODEN: PHREEB. ISSN: 0724-8741. Publisher: Plenum.

AB Interaction of human IgE with its high affinity receptor (FcεRI) on mast cells and basophils is an important step for initiating IgE mediated immune responses. To characterize the IgE and FcεRI interaction, the authors investigated this interaction in terms of stoichiometry and binding affinity in solution The binding of IgE and **IgE Fc**.epsilon.RI α chain, the extracellular portion of IgE high affinity receptor (sFcεFIα) was compared with the binding of IgE and IgE immunoadhesin (FcεRIα-IgG). The interaction was characterized by anal. ultracentrifugation, size exclusion chromatog., light scattering and ELISA. The authors show that the sFcεRIα is only able to bind to one IgE, while the immunoadhesin can bind to two IgE. The interaction between IgE and FcεRI is very strong. Both forms of soluble receptors have similar intrinsic binding affinity with IgE. Both soluble receptors (FcεRIα-IgG and sFcεRIα) can block the binding of IgE to its high affinity receptors on cell surface. The FcεRIα-IgG is a better IgE binding protein than sFcεRIα at physiol. relevant conditions. A humanized anti-IgE monoclonal antibody, rhuMAb E25 that also can block the binding of IgE to its high affinity receptors appears to bind to IgE at slightly different regions or in a different manner as the soluble forms of IgE receptors.

L11 ANSWER 26 OF 51 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1997:243736 Document No.: PREV199799542939. Rat basophilic leukaemia (RBL) cells overexpressing Rab3a have a reversible block in antigen-stimulated exocytosis. Smith, Janet; Thompson, Nicola; Thompson, Jeff; Armstrong, John; Hayes, Brian; Crofts, Andy; Squire, Jane; Teahan, Carmel; Upton, Louise; Solari, Roberto [Reprint author]. Cell Biol. Unit, Glaxo Wellcome Res. and Development Ltd., Med. Res. Centre, Gunnels Wood Road, Stevenage, Herts SG1 2NY, UK. Biochemical Journal, (1997) Vol. 323, No. 2, pp. 323-328.
ISSN: 0264-6021. Language: English.

AB The rat basophilic leukaemia (RBL) cell line has been widely used as a convenient model system to study regulated secretion in mast cells. Activation of these cells through the high-affinity receptor for **IgE** (**Fc**-epsilon-RI) results in degranulation and the extracellular release of mediators. There is good evidence of a role for GTPases in mast cell degranulation, and a number of studies with peptides derived from the Rab3a effector domain have suggested that Rab3a may function in this process. However, in neuroendocrine cells, overexpression of Rab3a can act as a negative regulator of stimulated exocytosis (Holz, Brondyk, Senter, Kuizon and Macara (1994) J. Biol.

Chemical 269, 10229-10234; Johanes, Lledo, Roa, Vincent, Henry and Darchen (1994) EMBO J. 13, 2029-2037). In order to study the function of Rab3a in RBL degranulation, we have generated clones of RBL cells stably expressing Rab3a, and show that in these haematopoietic cells Rab3a can also function as a negative regulator of exocytosis. Overexpression of a mutant form of Rab3a (Asn135 to Ile), which is predicted to be predominantly GTP-bound, also inhibited degranulation. However, overexpression of a mutant form of Rab3a that was truncated at the C-terminus to remove the sites for geranylgeranylation failed to inhibit degranulation. The effect of Rab3a is specific to secretion, and we observe no effect of Rab3a on receptor-mediated endocytosis. The Rab3a-induced block in degranulation can be bypassed by stimulation of streptolysin-O-permeabilized cells with guanosine 5'-(gamma-thio)triphosphate. We conclude from these studies that Rab3a is implicated in an early stage of granule targeting, whereas **fusion** of granules with the plasma membrane is regulated by a distinct downstream GTP-binding protein or proteins.

L11 ANSWER 27 OF 51 MEDLINE on STN DUPLICATE 5

97174301. PubMed ID: 9022035. Direct interaction of Syk and Lyn protein tyrosine kinases in rat basophilic leukemia cells activated via type I Fc epsilon receptors. Amoui M; Draberova L; Tolar P; Draber P. (Department of Mammalian Gene Expression, Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, Prague.) European journal of immunology, (1997 Jan) 27 (1) 321-8. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Activation of rat mast cells through the receptor with high affinity for **IgE** (**Fc** epsilonRI) requires a complex set of interactions involving transmembrane subunits of the Fc epsilonRI and two classes of nonreceptor protein tyrosine kinase (PTK). the Src family PTK p53/p56(lyn) (Lyn) and the Syk/ZAP-family PTK p72(syk) (Syk). Early activation events involve increased activity of Lyn and Syk kinases and their translocation into membrane domains containing aggregated Fc epsilonRI, but the molecular mechanisms responsible for these changes have remained largely unclear. To determine the role of Fc epsilonRI subunits in this process, we have analyzed Syk- and Lyn-associated proteins in activated rat basophilic leukemia (RBL) cells and their variants deficient in the expression of Fc epsilonRI beta or gamma subunits. Sepharose 4B gel chromatography of postnuclear supernatants from Nonidet-P40-solubilized antigen (Ag)- or pervanadate-activated RBL cells revealed extensive changes in the size of complexes formed by Lyn and Syk kinases and other cellular components. A **fusion** protein containing Src homology 2 (SH2) and SH3 domains of Lyn bound Syk from lysates of nonactivated RBL cells; an increased binding was observed when lysates from Ag- or pervanadate-activated cells were used. A similar amount of Syk was bound when lysates from pervanadate-activated variant cells deficient in the expression of Fc epsilonRI beta or gamma subunits were used, suggesting that Fc epsilonRI does not function as the only intermediate in the formation of the Syk-Lyn complexes. Further experiments have indicated that Syk-Lyn interactions occur in Ag-activated RBL cells under in vivo conditions and that these interactions could involve direct binding of the Lyn SH2 domain with phosphorylated tyrosine of Syk. The physical association of Lyn and Syk during mast-like cell activation supports the recently proposed functional cooperation of these two tyrosine kinases in Fc epsilonRI signaling.

L11 ANSWER 28 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6

97128467 EMBASE Document No.: 1997128467. Rat basophilic leukaemia (RBL) cells overexpressing Rab3a have a reversible block in antigen-stimulated exocytosis. Smith J.; Thompson N.; Thompson J.; Armstrong J.; Hayes B.; Crofts A.; Squire J.; Teahan C.; Upton L.; Solari R.. R. Solari, Cell Biology Unit, GiaxoWellcome Res. Development Ltd., Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, United Kingdom. Biochemical Journal 323/2 (321-328) 1997.
Refs: 47.

ISSN: 0264-6021. CODEN: BIJOAK. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The rat basophilic leukaemia (RBL) cell line has been widely used as a convenient model system to study regulated secretion in mast cells. Activation of these cells through the high-affinity receptor for **IgE** (**Fc**.epsilon.-RI) results in degranulation and the extracellular release of mediators. There is good evidence of a role for GTPases in mast cell degranulation, and a number of studies with peptides derived from the Rab3a effector domain have suggested that Rab3a may function in this process. However, in neuroendocrine cells, overexpression of Rab3a can act as a negative regulator of stimulated exocytosis. In order to study the function of Rab3a in RBL degranulation, we have generated clones of RBL cells stably expressing Rab3a, and show that in these haematopoietic cells Rab3a can also function as a negative regulator of exocytosis. Overexpression of a mutant form of Rab3a (Asn-135 to Ile), which is predicted to be predominantly GTP-bound, also inhibited degranulation. However, overexpression of a mutant form of Rab3a that was truncated at the C-terminus to remove the sites for geranylgeranylation failed to inhibit degranulation. The effect of Rab3a is specific to secretion, and we observe no effect of Rab3a on receptor-mediated endocytosis. The Rab3a-induced block in degranulation can be bypassed by stimulation of streptolysin-O-permeabilized cells with guanosine 5'-[γ-thio]triphosphate. We conclude from these studies that Rab3a is implicated in an early stage of granule targeting, whereas **fusion** of granules with the plasma membrane is regulated by a distinct downstream GTP-binding protein or proteins.

L11 ANSWER 29 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1996:487467 Document No. 125:140128 Binding of cynomolgus monkey IgE to a humanized anti-human IgE antibody and human high affinity IgE receptor. Meng, Y. Gloria; Singh, Naina; Wong, Wai Lee (Dep. BioAnalytical Technol., Genentech Inc., San Francisco, CA, 94080, USA). Molecular Immunology, 33(7/8), 635-642 (English) 1996. CODEN: MOIMD5. ISSN: 0161-5890. Publisher: Elsevier.

AB Antibodies which block IgE binding to its high affinity receptor have the therapeutic potential for treating allergic diseases. A humanized anti-human IgE antibody (E25) was developed for this purpose. Cynomolgus monkeys were used for preclin. studies of E25. We studied the binding of purified human IgE and cynomolgus monkey IgE to E25 and the human high affinity IgE receptor α-chain-IgG **fusion** mol. (FcεRI-IgG) by surface plasmon resonance. Human IgE and cynomolgus monkey IgE bound to immobilized E25 with similar affinity (apparent Kd = 0.06 and 0.19 nM, resp.). Human IgE and cynomolgus monkey IgE also bound to immobilized FcεRI-IgG with similar affinity (apparent Kd = 0.28 and 0.30 nM, resp.). These data suggest that the cynomolgus monkey is a valid model for preclin. studies of the E25 antibody and probably for other antibodies which block IgE binding to its receptor. An ELISA for measuring cynomolgus monkey IgE was developed to support preclin. studies. This ELISA used FcERI-IgG for capture and peroxidase labeled goat polyclonal antibody to human IgE for detection. Using purified cynomolgus monkey IgE as the standard, the serum IgE levels in six cynomolgus monkeys measured were 4-23 μg/mL.

L11 ANSWER 30 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1995:931315 Document No. 123:337475 Vaccines for treatment of IgE-mediated immune dysfunction and the control of IgE synthesis. Hurpin, Christian Marcel; Latour, Mireille Jeanne Marguerite (Pasteur Merieux Serums et Vaccins, Fr.). PCT Int. Appl. WO 9520606 A1 19950803, 47 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (French). CODEN: PIXXD2. APPLICATION: WO 1995-FR34 19950111. PRIORITY: FR 1994-846 19940126.

AB Vaccines useful for treating or preventing IgE mediated type 1

hypersensitivity reactions and inflammatory immune diseases, and for modulating IgE synthesis use a non-glycosylated or partially glycosylated polypeptide derived from the Fc fragment of human or primate IgE as the antigen. Specific antibodies induced by the immunogen of the vaccine composition, the immunogen used and a method for preparing same, are also disclosed. A number of antigenic peptides from the human **IgE** **Fc** CH2-CH4 region are identified and manufactured as **fusion** proteins with the trpE protein. Vervet monkeys inoculated s.c. with one of these peptides at 2 + 25 μg on day 0; 2 + 50 μg on day 15 and on day 30. At 45 days the animals showed significant titers of antibodies against the peptide. Control animals showed only a weak reaction to human IgE. Inoculated animals were more resistant to passive cutaneous anaphylaxis than control animals.

L11 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1995:272549 Document No. 122:53598 Interaction of p72syk with the γ and β subunits of the high-affinity receptor for immunoglobulin E, FcεRI. Shiue, Lily; Green, J.; Green, O. M.; Karas, Jennifer L.; Morgenstern, Jay P.; Ram, Mary K.; Taylor, Marta K.; Zoller, Mark J.; Zydowsky, Lynne D.; et al. (ARIAD Pharmaceuticals, Inc., Cambridge, MA, 02139, USA). Molecular and Cellular Biology, 15(1), 272-81 (English) 1995. CODEN: MCEBD4. ISSN: 0270-7306. Publisher: American Society for Microbiology.

AB Activation of protein tyrosine kinases is one of the initial events following aggregation of the high-affinity receptor for **IgE** (**Fc**.epsilon.RI) on RBL-2H3 cells, a model mast cell line. The protein tyrosine kinase p72syk (Syk), which contains two Src homol. 2 (SH2) domains, is activated and assocs. with phosphorylated FcεRI subunits after receptor aggregation. In this report, the authors used Syk SH2 domains, expressed in tandem or individually, as **fusion** proteins to identify Syk-binding proteins in RBL-2H3 lysates. The authors show that the tandem Syk SH2 domains selectively associate with tyrosine-phosphorylated forms of the γ and β subunits of FcεRI. The isolated C-proximal SH2 domain exhibited a higher affinity for the FcεRI subunits than did the N-proximal domain. When in tandem, the Syk SH2 domains showed enhanced binding to phosphorylated γ and β subunits. The conserved tyrosine-based activation motifs contained in the cytoplasmic domains of the γ and β subunits, characterized by 2 YXXL/I sequences in tandem, represent potential high-affinity binding sites for the dual SH2 domains of Syk. Peptide competition studies indicated that Syk exhibits a higher affinity for the phosphorylated tyrosine activation motif of the γ subunit than for that of the β subunit. In addition, the authors show that Syk is the major protein in RBL-2H3 cells that is affinity isolated with phosphorylated peptides corresponding to the phosphorylated γ subunit motif. Thus, Syk assocs. with the γ subunit of the high-affinity receptor for IgE through an interaction between the tandem SH2 domains of Syk and the phosphorylated tyrosine activation motif of the γ subunit and Syk may be the major signaling protein that binds to FcεRI tyrosine activation motifs in RBL-2H3 cells.

L11 ANSWER 32 OF 51 MEDLINE on STN

95145526. PubMed ID: 7531144. Recombinant CD4-IgE, a novel hybrid molecule, inducing basophils to respond to human immunodeficiency virus (HIV) and HIV-infected target cells. Krauss S; Kufer P; Federle C; Tabaszewski P; Weiss E; Rieber E P; Riethmuller G. (Institute for Immunology, University of Munich, Germany.) European journal of immunology, (1995 Jan) 25 (1) 192-9. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Basophils and mast cells, as the main effector cells in IgE-mediated type I hypersensitivity, are involved in the elimination of parasites and, according to recent findings, may also play an important role in the defense against bacterial and viral infections. Using a genetic engineering approach we wanted to redirect this potent IgE-mediated

defense system against intruding human immune deficiency virus. We constructed a recombinant CD4-IgE molecule, consisting of the two N-terminal domains of CD4 and the CH2-4 domains of the IgE heavy chain, thus providing the IgE with specificity for the gp120 of human immunodeficiency virus (HIV). The binding properties of hybrid CD4-IgE to the high-affinity receptor for **IgE** (**Fc** epsilon RI) on basophils as well as to the low-affinity receptor (Fc epsilon RII or CD23) for IgE on lymphoid cells were found to be similar to those of native IgE. At the same time, the CD4 domains of the recombinant molecule retained the gp120 binding specificity with an affinity similar to that of the native CD4. By functional tests, we demonstrated that CD4-IgE armed basophils can be triggered by free HIV and by HIV-infected cells to release their mediators. We further show that HIV-triggered basophils lead to a decreased replication of HIV in susceptible T cells. We, therefore, conclude that the type I hypersensitivity effector cells can be engaged in the elimination of HIV-infected cells, at least in vitro. Because of the strong binding of the CD4-IgE construct to the Fc epsilon RI, we assume that CD4-IgE has a short t1/2 in serum, but may similarly to IgE exhibit prolonged resident time on basophils and mast cells, which are located close to mucosal surfaces or in the connective tissue. Thus CD4-IgE could play an important role in the elimination of HIV also in vivo.

L11 ANSWER 33 OF 51 MEDLINE on STN
95067282. PubMed ID: 7976733. Characterization of the human **IgE Fc**-Fc epsilon RI alpha interaction. Kochan J P; Mallamaci M; Gilfillan A; Madison V; Basu M. (Department of Bronchopulmonary Research, Hoffmann-La Roche Inc., Nutley, NJ 07110.) Advances in experimental medicine and biology, (1994) 347 31-8. Journal code: 0121103. ISSN: 0065-2598. Pub. country: United States. Language: English.

AB A significant amount of progress has been achieved on characterizing the interaction of the **IgE Fc** molecule with the Fc epsilon RI alpha. However, there is yet no definitive structural information which precisely defines the nature of this interaction. It is clear that this information will only be provided by the resolution of the X-ray crystallographic structures of the **IgE Fc** molecule, the Fc epsilon RI alpha subunit extracellular domain, and the **IgE Fc**-Fc epsilon RI alpha complex. It is anticipated that these structures will be determined in the near future, and that they may provide some insight into the development of potential therapeutics effective in the management of IgE-mediated allergic diseases.

L11 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
1993:619205 Document No. 119:219205 Plasmids for secretory expression of allergy-inhibition chimera protein of human in Escherichia coli. Kitai, Kazuo (Teijin Ltd, Japan). Jpn. Kokai Tokkyo Koho JP 05176772 A2 19930720 Heisei, 11 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1992-747 19920107.

AB The plasmids contain chimeric gene for human IgE and IgG Fc regions under the regulation of an alkalophilic Bacillus promoter and signal sequence were constructed for secretory expression in E. coli. PEG2 containing a synthetic sequence of human **IgE Fc** region and sequence for human IgG Fc region of pEXFC10 was constructed. The plasmid was transformed into Escherichia coli by known method. The recombinant E. coli produced the chimera protein and secreted the chimera protein in the culture supernatant.

L11 ANSWER 35 OF 51 MEDLINE on STN
93293823. PubMed ID: 7685756. Purification and characterization of human recombinant **IgE-Fc** fragments that bind to the human high affinity IgE receptor. Basu M; Hakimi J; Dharm E; Kondas J A; Tsien W H; Pilson R S; Lin P; Gilfillan A; Haring P; Braswell E H; +. (Department of Protein Biochemistry, Roche Research Center, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.) Journal of biological chemistry, (1993 Jun 25) 268 (18) 13118-27. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The Fc-region of immunoglobulin E (IgE) comprising C epsilon 2, C epsilon 3, and C epsilon 4 domains is sufficient for binding to the alpha chain of the high affinity **IgE-Fc** receptor (Fc epsilon RI alpha). In order to identify the smallest Fc fragment capable of binding to the Fc epsilon RI alpha with high affinity, various regions of the **IgE-Fc** molecule were expressed in COS cells and investigated for their ability to bind Fc epsilon RI alpha. The smallest fragment that showed Fc epsilon RI alpha binding activity spans amino acids 329-547 and lacks the entire C epsilon 2 domain. Two active fragments, viz. Fc epsilon(315-547) (containing Cys328 which is responsible for interchain S-S bonding) and Fc epsilon(329-547), have been overexpressed in CHO cells and purified to homogeneity. The purified proteins bind to the Fc epsilon RI alpha with high affinity, similar to native IgE. SDS-polyacrylamide gel electrophoresis analyses indicate that Fc epsilon(315-547) is an S-S-linked dimer of apparent molecular mass of 68 kDa. Fc epsilon(329-547) appears on SDS-gel as three distinct bands at approximately 32 kDa, both under reducing and nonreducing conditions. However, size exclusion chromatography and analytical ultracentrifugation studies suggest that Fc epsilon(329-547) also remains associated as a dimer. The presence of N-linked glycosylation was detected in both proteins. The deglycosylated form of Fc epsilon(315-547) was isolated after Endo F/N-glycosidase F digestion and demonstrated to have binding activity comparable to that of the mock-digested protein. These results suggest that the presence of N-linked sugars is not necessary for Fc epsilon RI alpha binding. Both proteins blocked the release of histamine from RBL cells expressing human Fc epsilon RI alpha in a dose-dependent manner. The availability of these recombinant **IgE-Fc** proteins will be helpful in elucidating the key epitopes essential for the binding of IgE to its high affinity receptor.

L11 ANSWER 36 OF 51 MEDLINE on STN DUPLICATE 7
93359054. PubMed ID: 8354400. Receptor phage. Display of functional domains of the human high affinity IgE receptor on the M13 phage surface. Scarselli E; Esposito G; Traboni C. (Istituto di Ricerche di Biologia Molecolare P. Angeletti (IRBM), Pomezia, Italy.) FEBS letters, (1993 Aug 23) 329 (1-2) 223-6. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB In this paper we demonstrate that phage display technology is a suitable system for studying the interaction between the high-affinity receptor for **IgE** (**Fc** epsilon RI) and IgE. The alpha subunit extracellular domains of the human receptor were expressed on the surface of filamentous phage M13 fused to the carboxyl-terminal part of the gene III protein (pIII). Two constructs were made, the first with both the Ig-like domains of the receptor alpha chain and the second with only the C-terminal domain. The **fusion** genes were cloned in a phagemid vector to display monovalently the receptor on the phage surface. Our results indicate that the alpha receptor expressed on the phage is able to interact with IgE as demonstrated by an ELISA assay. In addition, by using the same system, we show that a single domain of the alpha receptor is sufficient for the interaction with IgE although with a binding affinity lower than that of the two-domain receptor.

L11 ANSWER 37 OF 51 MEDLINE on STN DUPLICATE 8
93270911. PubMed ID: 8499225. Fc epsilon RI and the T cell receptor for antigen activate similar signalling pathways in T cell-RBL cell hybrids. Marano N; Liotta M A; Slattery J P; Holowka D; Baird B. (Department of Biology, Middlebury College, VT 05753.) Cellular signalling, (1993 Mar) 5 (2) 155-67. Journal code: 8904683. ISSN: 0898-6568. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In order to investigate the functional similarities of the high affinity receptor for **IgE** (**Fc** epsilon RI) and the T cell receptor for antigen, we have developed a high efficiency polyethylene glycol-mediated **fusion** method to make somatic hybrids between cells from a mast cell line (RBL-2H3) and cells from T lymphoma cell lines (Jurkat and HPB-ALL). Using flow cytometry to select for the

heterologously fused cells, we demonstrated that aggregation of the T cell receptor results in the efficient secretion of [3H]5-hydroxytryptamine from RBL cell-derived granules. In addition, both receptors mediate Ca2+ mobilization in the hybrid cells that is insensitive to inhibition by the protein kinase C activator phorbol-12-myristoyl-13-acetate (PMA). In contrast, Ca2+ mobilization caused by aggregation of Fc epsilon RI in the parent RBL cells is completely inhibited by PMA. The results indicate that these two different receptors for foreign antigen can substitute for each other to trigger responses in the hybrid cells that are unique to each cell type. The methodology employed has general utility for studying signal transduction mediated by mammalian cell surface receptors.

L11 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
1993:5605 Document No. 118:5605 Monoclonal antibodies which bind to secreted and membrane-bound IgE, but not to IgE on basophils. Chang, Tse Wen; Davis, Frances M.; Gossett, Lani A.; Sun, Lee K.; Sun, Bill N. C.; Sun, Cecily R. Y.; Liou, Ruey S. (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9217207 A1 19921015, 22 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US1991 19910326.
AB Murine monoclonal antibody (MAb) TES-C21 and chimeric mouse/human MAb TESC-2, which has variable regions derived from TES-C21 and human (γ1,κ) constant regions, are disclosed which bind specifically to IgE and IgE-secreting B-cells. Neither MAb binds to IgE bound to **IgE Fc**.epsilon.RII receptors and both inhibit the binding of IgE to FcεRII receptors on B-cells. Neither MAb induces histamine release from human basophils. TESC-2 inhibits the binding of IgE to basophils. These properties make these MAbs well-suited for use in human allergy therapy.

L11 ANSWER 39 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 9
92287744 EMBASE Document No.: 1992287744. Establishment of a sensitive radioimmunoassay for the detection of human IgE-binding factor (soluble CD23). Yanagihara Y.; Kiniwa M.; Kajiwara K.; Shida T.. Clinical Research Center for Allergy, National Sagamihara Hospital, 18-1 Sakuradai,Sagamihara City, Kanagawa 228, Japan. International Archives of Allergy and Immunology 98/3 (189-199) 1992.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.
AB A monoclonal antibody (mAb) specific to low-affinity receptor for **IgE** (**Fc**.epsilon.RII/CD23) was established by the **fusion** of spleen cells of BALB/c mice immunized with the FcεRII+ human B lymphoblastoid cell line (RPMI 8866) with mouse myeloma P3U1. Four mAbs, 10/3 (IgG1), 11/4 (IgG1), 12/2 (IgG2b) and 15/6 (IgM), almost completely inhibited the IgE binding to FcεRII+ cells but not to FcεRII- cells. More directly, they were demonstrated to react only with 43-kD component/FcεRII of the cell lysate of RPMI 8866 cells by sodium dodecyl sulfate polyacrylamide gel electrophoresis and Western blot analysis. Since they have a different epitope specificity, a solid-phase radioimmunoassay (RIA) for the measurement of IgE-binding factor (IgE-BF) was established. It was found that the RIA with the use of 10/3 and 125I-labeled 11/4 or 12/2 gave good results in the detection of IgE-BF derived from B cells and monocytes as well as of T-cell-derived IgE-BF. More importantly, serum IgE-BF was also quantitatively measured by this RIA. Although increased serum levels of IgE-BF were observed in atopic patients, serum IgE-BF was decreased rather than increased in patients with very high serum IgE. This phenomenon may be explained by the decreased ability of the patients' B cells to spontaneously release IgE-BF in vitro.

L11 ANSWER 40 OF 51 MEDLINE on STN DUPLICATE 10
89229060. PubMed ID: 2540803. Implanted **IgE-Fc** epsilon

R complexes elicit IgE-mediated activation of RBL-2H cells. Ran S; Loyter A; Rivnay B. (Department of Membrane Research, Weizmann Institute of Science, Rehovot, Israel.) Biochemistry, (1989 Jan 24) 28 (2) 644-51. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB The high-affinity receptor for **IgE** (**Fc** epsilon R) is the cellular trigger of the antigen-induced activation of mast cells and basophils. To examine the functional integrity of Fc epsilon R, we have adopted a protein implantation procedure whereby the purified receptor complex was coreconstituted with Sendai virus envelopes. The latter promoted **fusion** of the hybrid vesicles with recipient cells such as rat basophilic leukemia, RBL-2H3, thus serving as a vehicle for the receptor. The implanted Fc epsilon R was complexed with 125I-labeled mouse IgE (anti-DNP) to permit receptor quantification as well as specific triggering by DNP20BSA. Implantation in the presence of unlabeled rat IgE, which blocked the native receptors on the recipient RBL-2H3 cells, resulted in incorporation of up to 15 ng of receptor-bound IgE/10(6) cells. This was roughly equivalent in amount to 10-20% of the native receptors on such cells. The exocytosis which was triggered in the recipient cells by reagents that specifically recognized the implanted IgE reached between 15 and 50% of the maximal response. Various treatments that interfered with the activities of the viral envelopes reduced both receptor incorporation (3-5-fold) and cell degranulation (3-10-fold). These included separation of the receptor from the reconstituted envelopes, addition of serum to the incubation mixture (to inhibit vesicle-cell binding), and trypsinization of the virus (to inhibit vesicle-cell **fusion**). Poly(ethylene glycol) 8000 (4%) enhanced both the incorporation of the receptor and its functional responses. These treatments distinguished between real incorporation of **IgE -Fc** epsilon R complexes and other mechanisms of 125I-IgE association with the recipient cells.(ABSTRACT TRUNCATED AT 250 WORDS)

L11 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1989:613327 Document No. 111:213327 Recombinant manufacture of human **IgE Fc** fragment. Ikeyama, Shuichi; Nishimura, Tadashi (Takeda Chemical Industries, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 63290899 A2 19881128 Showa, 9 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1987-123859 19870522.

AB A **fusion** protein comprising a human **IgE Fc** fragment (amino acids 226-365 or 226-400) and linker peptide(s) is manufactured by cultivating a recombinant Escherichia coli. Plasmid pGETtrp712 encoding the **fusion** protein comprising linker protein and **IgE Fc** fragment was used to transformed E. coli. The transformants were cultivated and 2 **IgE Fc** fragment-containing proteins, with an approx. mol. weight 20,000 and 18,000, resp., were recovered and purified by immunoaffinity chromatog.

L11 ANSWER 42 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1988:588798 Document No. 109:188798 Immunoaffinity column purification of recombinant **IgE Fc** fragment **fusion** proteins for use as an antiallergy medicine. Ikeyama, Shuichi; Nishimura, Osamu (Takeda Chemical Industries, Ltd., Japan). Eur. Pat. Appl. EP 269455 A2 19880601, 19 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1987-310475 19871127. PRIORITY: JP 1986-281871 19861128; JP 1987-232295 19870918.

AB Purification of recombinant **IgE Fc** fragment-interleukin-2 (IL-2) signal peptide **fusion** proteins using immunoaffinity chromatog. Mouse L cells transformed with pTB543, encoding a **fusion** protein comprising the IL-2 leader peptide, the 1st 11 N-terminal amino acids of IL-2, a small linker peptide, and the Fc portion of human IgE, were cultured. The **fusion** protein was purified from the medium using (NH4)2SO4 precipitation, immunoaffinity chromatog. (with a monoclonal antibody against IgE), and gel filtration chromatog. (Sephacryl

S-200). A pure glycosylated protein was obtained.

L11 ANSWER 43 OF 51 MEDLINE on STN DUPLICATE 11
88253447. PubMed ID: 3260137. Secretion of human EGF and IgE in mammalian cells by recombinant DNA techniques; use of a IL-2 leader sequence. Sasada R; Marumoto R; Igarashi K. (Central Research Division, Takeda Chemical Industries, Ltd., Osaka, Japan.) Cell structure and function, (1988 Apr) 13 (2) 129-41. Journal code: 7608465. ISSN: 0386-7196. Pub. country: Japan. Language: English.

AB Expression plasmids were constructed containing chemically synthesized human epidermal growth factor (EGF) gene fused in a frame to a leader sequence of human interleukin-2 (IL-2) gene under the control of a viral promoter. COS7 cells transfected with the plasmids synthesized and secreted EGF. Transfection of mouse A9 cells or BALB/3T3 clone A31 cells with the plasmids permitted the isolation of cell lines secreting the product which showed EGF activity. In particular, A31 transformed cells secreting human EGF grew well even in a medium containing a minimal level of serum. Using similar vectors having IgE cDNA (C2-C4) in place of EGF gene, a human **IgE Fc** fragment was also produced and secreted in mouse cells. These results show that heterologous leader sequences are useful for the expression and secretion of proteins whose genes lack leader sequences.

L11 ANSWER 44 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
1987:421676 Document No. 107:21676 Monoclonal antibody specific for T cell-derived human IgE binding factors. Kisaki, Tomonari; Huff, Thomas F.; Conrad, Daniel H.; Yodoi, Junji; Ishizaka, Kimishige (Good Samaritan Hosp., Johns Hopkins Univ., Baltimore, MD, USA). Journal of Immunology, 138(10), 3345-51 (English) 1987. CODEN: JOIMA3. ISSN: 0022-1767.

AB A B cell hybridoma secreting monoclonal antibody against human IgE binding factors was obtained by immunization of BALB/c mice with partially purified IgE binding factors, and **fusion** of their spleen cells with SP-2/0-AG14 cells. The monoclonal antibody bound all of the 60,000, 30,000, and 15,000 dalton IgE binding factors from 2 cell hybridomas and those from activated T cells of a normal individual. The antibody bound both IgE-potentiating factors and IgE-suppressive factors. However, the monoclonal anti-IgE-binding factor bound neither FcεR on RPMI 8866 cells nor IgE binding factors from the B lymphoblastoid cells. A monoclonal antibody against FcεR on B cells bound the 60,000 and 30,000 dalton IgE binding factors from both T cell hybridomas and RPMI 8866 cells but did not bind the 15,000 dalton IgE binding factors from either T cells or B cells. Thus, T cell-derived IgE binding factors have a unique antigenic determinant that is lacking in both FcεR on B cells and B cell-derived IgE binding factors. The anti-IgE binding factor and anti-FcεR monoclonal antibodies both failed to stain cell surface components of IgE binding factor-producing T cell hybridomas. However, both antibodies induced the T cell hybridoma to form IgE binding factors. Apparently, the T cell hybridomas bear low nos. of FcεR that share antigenic determinants with IgE binding factors secreted from the cells.

L11 ANSWER 45 OF 51 MEDLINE on STN DUPLICATE 12
87196428. PubMed ID: 2437203. Monoclonal antibodies specific to the alpha-subunit of the mast cell's Fc epsilon R block IgE binding and trigger histamine release. Baniyash M; Alkalay I; Eshhar Z. Journal of immunology (Baltimore, Md. : 1950), (1987 May 1) 138 (9) 2999-3004. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB In an attempt to block the interactions between IgE and its receptor on mast cells (Fc epsilon R), we have established anti-Fc epsilon R monoclonal antibodies (mAb) by **fusion** of myeloma cells with mouse splenocytes immunized with irradiated rat basophilic leukemia (RBL) cells. Two anti-Fc epsilon R mAb were obtained (denoted 4.7 and 5.14) that could specifically bind to RBL and mast cells. This binding could be inhibited by IgE. The mAb and their F(ab')2 fragments inhibited 125I-IgE

binding to RBL cell and triggered cell degranulation. The Fab' fragments, on the other hand, could only inhibit IgE binding but did not stimulate cell degranulation. Furthermore, these monovalent fragments inhibited RBL and mast cell degranulation induced by IgE-antigen complexes both in vitro and in vivo in the passive cutaneous anaphylaxis reaction. The number of mAb 4.7 and 5.14 molecules bound per RBL cells was similar to that of IgE; nevertheless, mAb 4.7 and 5.14 recognized different epitopes on the IgE receptor. Immunoprecipitation and immunoblotting analysis demonstrated that the mAb reacted with the alpha-subunit of the Fc epsilon R. Our findings establish the anti-Fc epsilon R mAb as a useful reagent for the isolation and characterization of the Fc epsilon R's alpha-subunit and the monomeric (Fab') for blocking the **IgE-Fc** epsilon R interactions.

L11 ANSWER 46 OF 51 MEDLINE on STN DUPLICATE 13

86225491. PubMed ID: 2940297. Murine B cell hybridomas bearing ligand-inducible Fc receptors for IgE. Lee W T; Conrad D H. Journal of immunology (Baltimore, Md. : 1950), (1986 Jun 15) 136 (12) 4573-80. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Interest in the regulation of IgE synthesis has generated investigation of low-affinity Fc receptors for **IgE** (**Fc** epsilon R) and the related immunoregulatory IgE-binding factors. In an effort to facilitate biochemical analysis of the B lymphocyte Fc epsilon R, hybridoma technology has been used to create stable cell lines that maintain Fc epsilon R in high numbers. **Fusion** of the HAT-sensitive B lymphoma, M12.4.5, with murine B cells from Nippostrongylus brasiliensis infected BALB/c mice led to the formation of hybrid cells of B cell phenotype, all of which were Fc epsilon R+, including several that had greater than 50,000 Fc epsilon R/cell. The Fc epsilon R on these cells were biochemically identical to the Fc epsilon R on normal B cells with respect to binding affinity (approximately equal to 10(8) M-1), m.w. (49,000), and tryptic peptides. Each hybridoma cell line specifically increased its Fc epsilon R level between twofold and fourfold when cultured with rat or mouse IgE. Additional studies demonstrated that the increased IgE binding ability was due to an increase in receptor number rather than an affinity change, and the Fc epsilon R increase was seen on the entire cell population. Dose studies indicated that oligomeric IgE was 10-fold more effective than monomeric IgE in causing upregulation, and the effective concentrations required indicated that induction occurred only if IgE was present in saturating concentrations. Upon addition of IgE, peak Fc epsilon R levels were reached after 15 to 20 hr of culture; blocking protein synthesis with cycloheximide largely blocked the increase in Fc epsilon R levels. Additionally, the inductive signal IgE must constantly be present to maintain upregulated Fc epsilon R levels in that its removal from the culture resulted in a rapid decline of Fc epsilon R from induced to normal levels. Because Fc receptor upregulation is important to several systems describing Ig isotype-specific regulation, the ability to examine such receptor upregulation at a clonal level should aid in discerning the role of the Fc epsilon R in the regulation of IgE antibody synthesis.

L11 ANSWER 47 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

1986:531811 Document No. 105:131811 Monoclonal antibody (H107) inhibiting IgE binding to FCεR(+) human lymphocytes. Noro, Nobuhiro; Yoshioka, Akira; Adachi, Mitsunobu; Yasuda, Kazuhiko; Masuda, Tohru; Yodoi, Junji (Fac. Med., Kyoto Univ., Kyoto, Japan). Journal of Immunology, 137(4), 1258-63 (English) 1986. CODEN: JOIMA3. ISSN: 0022-1767.

AB A hybridoma producing monoclonal antibody blocking the binding of human IgE to lymphocyte Fc receptors (FcεR) was established by the **fusion** of murine myeloma cells P3X63.653.Ag8 with BALB/c spleen cells immunized with FcεR(+) human B lymphoblastoid cell line cells, RPMI1788. A clone of the hybridoma (H107) produced a monoclonal IgG2b antibody that inhibited the rosette formation of FcεR(+)

human B lymphoblastoid cell line cells (RPMI1788, RPMI8866, CESS, Dakiki, and IM9) with fixed ox red blood cells (ORBC) conjugated with human IgE (IgE-ORBC). In contrast, the rosette formation with IgG-conjugated ORBC (IgG-ORBC) on FcγR(+), FcεR(-) Daudi cells were not affected by the H107 antibodies. A close association of FcεR and the antigenic determinant recognized by H107 antibody was suggested by the following results. First, the bindings of 125I-labeled IgE (125I-IgE) or 125I-labeled H107 IgG2b antibody (125I-H107) to RPMI8866 cells were inhibited by cold human IgE and H107 IgG2b but not by other classes of human Ig (IgA and IgG), MPC11 IgG2b, or unrelated monoclonal antibodies. Second, H107 antibody reacted with FcεR(+) B cell lines but not with FcεR(-) B cell lines as determined by indirect immunofluorescence. Third, FcεR(+) cells were depleted by incubation in a dish coated with H107 antibody or IgE but not in a dish coated with unrelated antibodies. Finally, there was a correlation between the increase of FcεR(+) cells and that of H107(+) cells in peripheral blood lymphocytes of patients with atopic dermatitis. The surface antigens on FcεR(+) RPMI8866 cells recognized by H107 antibodies had a mol. size of 45,000.

L11 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
1986:128114 Document No. 104:128114 Manufacture of monoclonal antibody against class-specific Fcε receptor by hybridoma cells. Yodoi, Junji; Noro, Norihiro; Yoshioka, Akira (Nichirei Corp., Japan). Jpn. Kokai Tokkyo Koho JP 60255734 A2 19851217 Showa, 3 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1984-108643 19840530.

AB A monoclonal antibody against class-specific Fcε receptor is manufactured by a hybridoma cell line which is produced by conventional cell **fusion** of a mouse P3+63.653 cell and a spleen cell isolated from a mouse which had been immunized with Fcε (+) human B cell. The monoclonal antibody has the following characteristics: (1) it can specifically recognize antihuman IgE class-specific Fc receptor; (2) inhibits rosette formation of FcεR(+) human B cells with human IgE-coated, formalin-fixed bovine erythrocytes; (3) it is nonreactive with anti-human Ia antigen; (4) it reacts pos. with exterminal blood lymphocytes of allergic patients with a high IgE blood-level, but is non-reactive with normal human lymphocytes.

L11 ANSWER 49 OF 51 MEDLINE on STN DUPLICATE 14
85158642. PubMed ID: 3980883. Exercise-induced anaphylaxis: a serious form of physical allergy associated with mast cell degranulation. Sheffer A L; Tong A K; Murphy G F; Lewis R A; McFadden E R Jr; Austen K F. Journal of allergy and clinical immunology, (1985 Apr) 75 (4) 479-84. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB Exercise-induced anaphylaxis (EIA) is a unique and an increasingly recognized syndrome consisting of premonitory symptoms and signs of generalized body warmth, pruritus, and erythema, which progresses on continued exertion to confluent urticaria, laryngeal edema with stridor or hoarseness, and gastrointestinal colic and frequently culminates in vascular collapse. Previous studies of five individuals with this condition have demonstrated significant elevations of serum histamine concurrent with the early clinical manifestations after experimental exercise. To assess relevant morphologic alterations in the skin of these patients, cutaneous mast cells were examined by light and transmission electron microscopy before and during the initial erythema elicited by exertion. The marked alterations observed in mast cells immediately after exercise consisted of (1) loss of electron density and internal substructure of granules, (2) **fusion** of granule membranes with those of adjacent granules and with mast cell membranes creating conduits to the extracellular space, and (3) an apparent decrease in the number of intact granules per cell. Biopsy specimens obtained before exercise from patients with EIA and from two normal individuals who served as control subjects were identical, and the control subjects had normal mast cell morphology after exercise. Serum histamine levels were significantly elevated in patients with EIA after exercise at the time of biopsy,

whereas control subjects had normal levels. These observations provide evidence that EIA is a distinct form of physical allergy associated with mast cell degranulation similar in morphology to that of human pulmonary mast cell **IgE-Fc**-dependent activation secretion.
Characterization of this disorder is important because its prevalence may be underestimated, and its clinical consequences, which may include some morbidity, are not fully known.

L11 ANSWER 50 OF 51 MEDLINE on STN DUPLICATE 15
85003774. PubMed ID: 6207029. Inhibition of IgE binding to mast cells and basophils by monoclonal antibodies to murine IgE. Baniyash M; Eshhar Z. European journal of immunology, (1984 Sep) 14 (9) 799-807. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.
AB In an attempt to identify the site on IgE which binds with high affinity to the Fc epsilon receptor (Fc epsilon R) on mast cells, we established monoclonal anti-IgE antibodies (mAb) by **fusion** of myeloma cells with rat splenocytes immunized with purified murine IgE mAb. Six individual mAb were found to react with various IgE mAb of different specificities and not with immunoglobulins of other classes. Three different clusters of epitopes on the Fc epsilon portion could be detected by antibody competition studies. These antigenic determinants were expressed on the Fc epsilon portion and required the two heavy chains in their native conformation. Two groups of mAb and their Fab' fragments completely inhibited the binding of 125I-labeled IgE to rat basophilic leukemia cells (RBL), and one mAb inhibited the specific IgE binding only partially (55-65%). Likewise, the Fab' fragments of the purified mAb inhibited the antigen-mediated, IgE-dependent, serotonin release of RBL cells. These in vitro findings were confirmed by in vivo experiments, which demonstrated that the anti-IgE mAb could specifically block passive cutaneous anaphylaxis reaction when injected i.d., before challenging with the antigen. The differences in blocking reactivity of the various anti-IgE mAb are discussed in view of heterogeneity in the **IgE-Fc** epsilon R interaction.

L11 ANSWER 51 OF 51 EMBASE
on STN
84088309 EMBASE Document No.: 1984088309. Role of cyclic nucleotides in the activation-secretion response. Winslow C.M.; Austen K.F.. Department of Medicine, Harvard Medical School, Boston, MA 02115, United States.
Progress in Allergy VOL. 34/- (236-270) 1984.
CODEN: PRALAD. Pub. Country: Switzerland. Language: English.
AB **IgE-Fc** receptor perturbation in the mast cell initiates a complex series of biochemical events which occur in parallel and in sequence. A transient monophasic rise in cAMP is necessary for degranulation to occur, as indicated by inhibition of this rise and of mediator by adenylate cyclase 'P' site inhibitors. The second messenger function of cAMP in mast cell activation-secretion is defined by activation of cAMP-dependent protein kinases and suppression of this effect by 'P' site inhibitors. Thus perturbation of the membrane IgE receptor is transmembrane-linked to adenylate cyclase, which generates cAMP to activate cytoplasmic cAMP-dependent protein kinase. Conversely, activation of cytoplasmic cAMP-dependent protein kinases by phosphodiesterase inhibitors suppresses mediator release. The specific facilitory and down-regulatory phosphorylation events in the mast cell activation-secretion response are unknown at this time. The possible facilitory effects could be at the contractile or cytoskeletal level, in phosphorylation of myosin light-chain subunits, microtubule-associated protein, or tubulin subunits. Ca2+-transport into the cell might be accompanied by phosphorylation of Ca2+-Mg2+ ATPase. Phospholipid turnover would be increased by inactivation, through phosphorylation of the inhibitor of phospholipase A2, macrocortin, leading to products taking part in membrane fluidity, calcium influx, and membrane **fusion.**
Although high levels of cAMP inhibit mediator release, their mechanism of action is unknown. Phosphorylation of myosin light-chain kinase inhibits

contraction and movement of granules to the cell surface. Mobilization of calcium from intracellular pools could be inhibited by phosphorylation of a protein that sequesters Ca2+. cAMP appears to inhibit phospholipd metabolism; but it has not been demonstrated which, if any enzymes involved in phospholipid turnover are phosphorylated by protein kinases as part of down-regulation. It may be found that the 78,000-dalton protein phosphorylated in a Ca2+-dependent fashion is also a substrate for a cAMP-dependent protein kinase, and enters into inhibition of phospholipid turnover.

=> s chimeric protein
L12 36231 CHIMERIC PROTEIN

=> s l12 and Fc fusion
L13 203 L12 AND FC FUSION

=> s l13 and myelin basic protein
L14 0 L13 AND MYELIN BASIC PROTEIN

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PROCESSING COMPLETED FOR L13
L15 177 DUP REMOVE L13 (26 DUPLICATES REMOVED)

=> s l15 and autoantigen
L16 4 L15 AND AUTOANTIGEN

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PROCESSING COMPLETED FOR L16
L17 4 DUP REMOVE L16 (0 DUPLICATES REMOVED)

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L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:656809 Document No. 139:196279 **Chimeric proteins** comprising **autoantigen** epitope and effector molecule epitope for preventing and treating autoimmune diseases. Zocher, Marcel; Dreier, Torsten; Baeuerle, Patrick (Micromet A.-G., Germany). PCT Int. Appl. WO 2003068822 A2 20030821, 141 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP1389 20030212. PRIORITY: EP 2002-3332 20020213.

AB The present invention relates to a (poly)peptide construct consisting of at least two domains of at least two pluralities of domains wherein one of said domains or pluralities of domains comprises a de-immunized autoreactive antigen or (a) fragment(s) thereof specifically recognized by the Ig receptors of an autoreactive B-cells and wherein a/the further domain or plurality of domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes. Preferably, said (poly)peptide construct consisting of at least two domains comprises a de-immunized autoreactive antigen or (a) fragment which is MOG or (a) fragment(s) thereof and a second domain comprising an effector mol. is an anti-CD3 receptor or an Fc-part of an Ig. The invention also relates to compns. comprising the compds. of the invention. Described is also the use of the afore-mentioned (poly)peptide construct and further compds. for the preparation of a pharmaceutical composition for the treatment and/or prevention of an autoimmune disease. In addition, the present invention relates to method for treating, ameliorating and/or preventing of an autoimmune disease. Thus,

MOG-CD3, MOG-Fc, mutated MOG-Fc and AchR-**Fc fusion** proteins were prepared for eliminating autoreactive B cells.

L17 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:607428 Document No. 139:146195 Affinity purification of individual molecules, organelles, cells and other entities using affinity ligands immobilized via a nucleic acid-binding domain. Cherkasky, Alexander (Germany). Ger. Offen. DE 10202191 A1 20030807, 38 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2002-10202191 20020122.
AB A simple and user-friendly method of affinity purification of biol. entities for, diagnostics, proteomics and structural anal. is described. The method uses a protein that is an affinity ligand for a target protein in a fusion protein with a nucleic acid-binding protein. The nucleic acid-binding protein may bind with or without sequence specificity and it is used to bind the fusion protein to a matrix carrying an appropriate nucleic acid ligand. The affinity capture material is mixed with a solution or suspension containing the material of interest and is recovered by any appropriate method with the target material attached. The affinity capture material may be immobilized on a needle point.

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2001:904738 Document No. 136:36346 Soluble CD1 antigens. Gumperz, Jenny E.; Brenner, Michael B.; Behar, Samuel M. (The Brigham and Women's Hospital, Inc., USA). PCT Int. Appl. WO 2001094949 A2 20011213, 88 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18178 20010605. PRIORITY: US 2000-PV209416 20000605.
AB The authors disclose the preparation and characterization of CD1 fusion proteins. In one example, a soluble CD1d antigen was shown to present α-galactosylceramide to CD1-restricted T-cells. In a second example, the recognition of tumor phospholipids by CD1-restricted T-cells was demonstrated.

L17 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2001:798070 Document No. 135:343299 Bispecific opsonins. Himawan, Jeff (Elusys Therapeutics, Inc., USA). PCT Int. Appl. WO 2001080883 A1 20011101, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13161 20010424. PRIORITY: US 2000-PV199903 20000426; US 2000-PV244812 20001101.
AB The author discloses bispecific mols. that are characterized by having a first domain which binds an antigen and a second domain which binds the C3b-like receptor (known as complement receptor 1 (CR1) or CD35 in primates). In one example, a bispecific antibody is prepared that targets both IgE and the C3b receptor.

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L19          4 DUP REMOVE L18 (0 DUPLICATES REMOVED)

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L19 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:656809 Document No. 139:196279 **Chimeric proteins** comprising autoantigen epitope and effector molecule epitope for

preventing and treating autoimmune diseases. Zocher, Marcel; Dreier, Torsten; Baeuerle, Patrick (Micromet A.-G., Germany). PCT Int. Appl. WO 2003068822 A2 20030821, 141 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP1389 20030212. PRIORITY: EP 2002-3332 20020213.

AB The present invention relates to a (poly)peptide construct consisting of at least two domains of at least two pluralities of domains wherein one of said domains or pluralities of domains comprises a de-immunized autoreactive antigen or (a) fragment(s) thereof specifically recognized by the Ig receptors of an autoreactive B-cells and wherein a/the further domain or plurality of domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes. Preferably, said (poly)peptide construct consisting of at least two domains comprises a de-immunized autoreactive antigen or (a) fragment which is MOG or (a) fragment(s) thereof and a second domain comprising an effector mol. is an anti-CD3 receptor or an Fc-part of an Ig. The invention also relates to compns. comprising the compds. of the invention. Described is also the use of the afore-mentioned (poly)peptide construct and further compds. for the preparation of a pharmaceutical composition for the treatment and/or prevention of an autoimmune disease. In addition, the present invention relates to method for treating, ameliorating and/or preventing of an autoimmune disease. Thus, MOG-CD3, MOG-Fc, mutated MOG-Fc and AchR-**Fc fusion** proteins were prepared for eliminating autoreactive B cells.

L19 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

2003:203313 Document No. 138:233055 Protein and cDNA sequences of human and mouse interleukin 21 receptor MU-1 involved in the STAT5 signaling pathway, and their therapeutic use in inhibiting immune response. Carter, Laura; Whitters, Matthew J.; Collins, Mary; Young, Deborah A.; Donaldson, Debra D.; Lowe, Leslie D.; Unger, Michelle (USA). U.S. Pat. Appl. Publ. US 2003049798 A1 20030313, 26 pp., Cont.-in-part of U.S. Ser. No. 569,384. (English). CODEN: USXXCO. APPLICATION: US 2001-972218 20011004. PRIORITY: US 1998-40005 19980317; US 2000-560766 20000428; US 2000-569384 20000511.

AB Polynucleotides encoding the MU-1 hematopoietin receptor superfamily chain and fragments thereof are disclosed. Specifically, the protein and cDNA sequences for human and mouse interleukin 21 receptor MU-1 are provided. The invention also relates to recombinant production of MU-1 proteins. The invention also relates to tissue distribution of human and mouse cytokine receptor MU-1. The invention demonstrated that signaling through MU-1 results in phosphorylation of STAT5. MU-1 proteins and methods for their production are also disclosed.

L19 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

2002:595105 Document No. 137:153813 Generation and identification of monoclonal antibodies to human antigens. Nancy, Chang (Tanox, Inc., USA). PCT Int. Appl. WO 2002061389 A2 20020808, 22 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2796 20020201. PRIORITY: US 2001-PV265701 20010201.

AB A method of determining the antigens encoded by a genomic or cDNA library is

disclosed. Dendritic or other antigen presenting cells are transfected with DNA fragments in a vector which includes a signal peptide coding sequence and an sequence which encodes a peptide binding to a receptor on the antigen presenting cell. The expressed DNA fragments are secreted under control of the signal peptide, and bind to a cell surface receptor. The antigen presenting cells are used to generate monoclonal antibodies. The monoclonal antibodies may be screened by cloning the same fragments into a display vector containing a transmembrane domain thereby displaying the expressed proteins on the surface of a host cell. The monoclonal are screened against these displayed proteins for a pos. match.

L19 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2002:755100 Document No. 137:274170 A new member of the disintegrin family, zdint5, useful for modulating extracellular matrix interaction as anti-angiogenic factors. Holloway, James L.; Sheppard, Paul O.; Yamamoto, Gayle (USA). U.S. Pat. Appl. Publ. US 2002142439 A1 20021003, 37 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-781080 20010209. PRIORITY: US 2000-PV181511 20000210.

AB The present invention relates to polynucleotide and polypeptide mols., and variants thereof, for zdint5, a novel member of the Disintegrin Proteases. In particular, a member of the METH subfamily of proteins designated zdint5 METHs (Metalloprotease and Thrombospondin-1 repeat proteins) subfamily, designated as zdint5, is identified by domain sequence homol. search. Domains of zdint5 include: a metalloprotease domain, and two TSP1-like (Thrombospondin-1) domains. The polypeptides, and polynucleotides encoding them, are cell-cell interaction modulating and may be used for delivery and therapeutics. The present invention also includes antibodies to the zdint5 polypeptides.

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L20          4 L15 AND "MBP"

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L21          4 DUP REMOVE L20 (0 DUPLICATES REMOVED)

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L21 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:656809 Document No. 139:196279 **Chimeric proteins** comprising autoantigen epitope and effector molecule epitope for preventing and treating autoimmune diseases. Zocher, Marcel; Dreier, Torsten; Baeuerle, Patrick (Micromet A.-G., Germany). PCT Int. Appl. WO 2003068822 A2 20030821, 141 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP1389 20030212. PRIORITY: EP 2002-3332 20020213.

AB The present invention relates to a (poly)peptide construct consisting of at least two domains of at least two pluralities of domains wherein one of said domains or pluralities of domains comprises a de-immunized autoreactive antigen or (a) fragment(s) thereof specifically recognized by the Ig receptors of an autoreactive B-cells and wherein a/the further domain or plurality of domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes. Preferably, said (poly)peptide construct consisting of at least two domains comprises a de-immunized autoreactive antigen or (a) fragment which is MOG or (a) fragment(s) thereof and a second domain comprising an effector mol. is an anti-CD3 receptor or an

Fc-part of an Ig. The invention also relates to compns. comprising the compds. of the invention. Described is also the use of the afore-mentioned (poly)peptide construct and further compds. for the preparation of a pharmaceutical composition for the treatment and/or prevention of an autoimmune disease. In addition, the present invention relates to method for treating, ameliorating and/or preventing of an autoimmune disease. Thus, MOG-CD3, MOG-Fc, mutated MOG-Fc and AchR-**Fc fusion** proteins were prepared for eliminating autoreactive B cells.

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L22 28 L15 AND AUTOIMMUNE

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L23 28 DUP REMOVE L22 (0 DUPLICATES REMOVED)

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ENTER ANSWER NUMBER OR RANGE (1):1-28

L23 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2004:857429 Notch signalling modulation using a KLF and its effectors, diagnostic assays and therapeutics for **autoimmune** and inflammatory disorders. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004087195 A2 20041014, 150 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB1379 20040329. PRIORITY: GB 2003-7472 20030401.
AB A method is described for detecting, measuring or monitoring Notch signalling by determining the amount of a KLF (Kruppel-like factor) protein, or determining the amount of a polynucleotide coding for KLF. Methods of modulating the immune system by modulation of KLF activity and methods of modulating immune cell quiescence and proliferation are also described. A preferred KLF is human KLF-2, also known as LKLF (Q9Y5W3, NM_016270). Modulators of the Notch signalling pathway also comprise Notch ligands, such as Delta or Jagged, and DSL, EGF-like or extracellular domains thereof and polynucleotides coding for such proteins. Sequences of Delta-1/Ig-**Fc fusion** proteins are provided. Notch signaling pathway modulation was demonstrated in mouse model.

L23 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2004:162573 Document No. 140:223257 Methods for treating RAGE (receptor for advanced glycation end products)-associated disorders using fusion products of RAGE-LBE domain with Ig element, and genetic constructs encoding same. Pittman, Debra D.; Clancy, Brian; Larsen, Glenn; Trepicchio, William L.; Brennan, Fionula Mary; Feldmann, Marc; Foxwell, Brian John Maurice; Feldman, Jeffrey L. (Wyeth, John, and Brother Ltd., USA). PCT Int. Appl. WO 2004016229 A2 20040226, 100 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,

ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US25996 20030818. PRIORITY: US 2002-PV404205 20020816.

AB Fusion proteins comprising a Receptor for Advanced Glycation End Products Ligand Binding Element (RAGE-LBE) and an Ig element are disclosed. A RAGE-LBE may be any extracellular portion of a RAGE protein that retains the ability to bind to a RAGE ligand. Also disclosed are fusion proteins comprising a RAGE-LBE and a dimerization domain. Also disclosed are nucleic acids encoding such fusion proteins and methods for using disclosed nucleic acids and proteins to, for example, treat RAGE-related disorders, such as arthritis. Addnl. compns. and methods are also disclosed.

L23 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2004:817393 Document No. 141:289046 Method for treating **autoimmune** and alloimmune diseases. Miller, Richard G.; Rabinovich, Brian (Vasogen Ireland Limited, Ire.). U.S. US 6800300 B1 20041005, 7 pp. (English). CODEN: USXXAM. APPLICATION: US 2000-541033 20000331.

AB Disclosed is a method for treating a mammalian subject suffering from an **autoimmune** or alloimmune disease by administering to the subject a drug treatment which results in at least partial remission of one or more symptoms of the **autoimmune** or alloimmune disease, and administering to the subject autologous mammalian blood which has been modified extracorporeally by exposure to at least one stressor selected from an oxidative environment, an electromagnetic emission and a temperature above or below body temperature The modified mammalian blood is administered to the subject in an amount which is sufficient to maintain the remission of the symptoms of the **autoimmune** or alloimmune disease. A short course of treatment with TNF-α inhibitor p75 TNFR:Fc inhibited progression and caused remission of the symptoms of rheumatoid arthritis in rats, with decreased TNF-α activity being observed in animals treated with p75 TNFR:Fc. Following the treatment with p75 TNFR:Fc, the animals were injected with donor animal blood that had been heated to 42°, and at that temperature irradiated with UV light, principally at a wavelength of 254 nm, while a gas mixture of medical grade oxygen containing 14 μg/mL of ozone was bubbled through the blood at a flow rate of 240±24 mL/min. The combination therapy brought about remission and prevented reappearance of the symptoms of the disease.

L23 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2004:552972 Document No. 141:276100 Control of spontaneous B lymphocyte autoimmunity with adenovirus-encoded soluble TACI. Liu, Weimin; Szalai, Alex; Zhao, Limin; Liu, Di; Martin, Flavius; Kimberly, Robert P.; Zhou, Tong; Carter, Robert H. (University of Alabama at Birmingham, Birmingham, AL, USA). Arthritis & Rheumatism, 50(6), 1884-1896 (English) 2004. CODEN: ARHEAW. ISSN: 0004-3591. Publisher: John Wiley & Sons, Inc..

AB Serum B lymphocyte stimulator (BLyS) is increased in **autoimmune** diseases, both in animal models and in humans. This study examined the effect of BLyS blockade in 3 animal models of lupus. Antibodies and lupus-like disease manifestations were examined in mice after administration of a single injection of an adenoviral construct for the transmembrane activator and CAML interactor receptor (AdTACI) that produces high serum levels of TACI-**Fc fusion** protein. In C57BL/6 (B6) lpr/lpr mice (B6.lpr/lpr), which were used to model autoimmunity in the absence of severe disease, treatment of younger mice with AdTACI prevented the development of hypergammaglobulinemia. In contrast, use of AdTACI for BLyS blockade had only transient effects on the levels of IgG in normal B6 mice. AdTACI blocked the development of autoantibodies in younger B6.lpr/lpr mice and reversed the production of autoantibodies in older B6.lpr/lpr mice, and also reduced the nos. of splenic plasma cells. In MRL.lpr/lpr mice, which were used to examine disease manifestations, AdTACI reduced the extent of glomerulonephritis and proteinuria and improved survival, but had little effect on T cell infiltration and interstitial nephritis. However, in (NZB + NZW)F1 mice, AdTACI

induced neutralizing anti-TACI antibodies and failed to reduce the nos. of B cells. BLyS blockade has little effect on IgG levels in normal mice, but reverses the production of spontaneously produced IgM and IgG autoantibodies in the setting of established autoimmunity. Blockade of BLyS ameliorates B cell-dependent disease manifestations even in the MRL.lpr/lpr model, but its effectiveness on autonomous T cell aspects of the disease is limited. Moreover, its effectiveness is neutralized by anti-TACI antibodies when present. These results provide a basis for understanding the potential effects of BLyS blockade in human disease.

L23 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2004:502044 Document No. 141:122199 A Novel Therapy of Murine Collagen-Induced Arthritis with Soluble T1/ST2. Leung, Bernard P.; Xu, Damo; Culshaw, Shauna; McInnes, Iain B.; Liew, Foo Y. (Division of Immunology, Infection, and Inflammation and Centre for Rheumatic Diseases, Royal Infirmary, University of Glasgow, Glasgow, G11 6NT, UK). Journal of Immunology, 173(1), 145-150 (English) 2004. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.
AB Rheumatoid arthritis is characterized by chronic inflammatory infiltration of the synovium, leading to eventual cartilage and bone destruction. Previously, we have reported that soluble T1/ST2 (sST2), a member of the IL-1R gene family, inhibits LPS-induced macrophage proinflammatory cytokine production In this study, we report the therapeutic effect of sST2-Fc in the murine model of collagen-induced arthritis. A short term administration of sST2-**Fc fusion** protein significantly attenuated disease severity compared with controls treated with normal IgG. Histol. examination revealed that while control IgG-treated mice developed severe cellular infiltration in the joints, synovial hyperplasia, and joint erosion, this pathol. was profoundly reduced in sST2-Fc-treated animals. Treatment of sST2-Fc also down-regulated serum levels of IL-6, IL-12, and TNF-α. Spleen cells from the sST2-Fc-treated mice produced significantly less IFN-γ, TNF-α, IL-6, and IL-12 compared with cells from the control mice when cultured with collagen in vitro. Finally, pretreatment with ST2-Fc markedly inhibited the ability of human monocytic THP1 cells to release TNF-α when cocultured with peripheral blood T cells from rheumatoid patients. These results demonstrate that sST2-Fc may provide a novel approach in treating chronic **autoimmune** conditions by inhibiting the release of proinflammatory cytokines.

L23 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2003:796748 Document No. 139:302036 Novel OX40R binding peptides derived from extracellular domain of OX40L for the inhibition of OX40R-OX40L interaction, and therapeutic and diagnostic use thereof. Soto Jara, Claudio; Pena Rossi, Claudia (Applied Research Systems Ars Holding N.V., Neth. Antilles). PCT Int. Appl. WO 2003082919 A2 20031009, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP50089 20030402. PRIORITY: EP 2002-100334 20020403.
AB The present invention discloses peptides isolated from the extracellular domain of OX40 Ligand (OX40L) capable of binding OX40 Receptor (OX40R) and inhibiting OX40R-OX40L interaction. Such peptides, fusion proteins comprising them, as well as peptides and other mols. designed on their sequences, can be used as OX40R binding agents competing with natural OX40L for blocking OX40R-mediated cell signaling in the prophylaxis and/or treatment of diseases related to activated T cells. In particular, disclosed are peptides derived from the extracellular domain (P5, corresponding to residue 94-124, P5-1a:107-111, P5-1:107-116) from OX40L (also known as CD134 antigen ligand), that interact with OX40R with high

affinity and compete with OX40L. This binding activity has been tested using in vitro assays employing recombinant forms of OX40R (OX40R-IgG1) and OX40L (OX40L-CD8). OX40L and OX40R, and demonstrating that OX40L can be effectively competed by the claimed peptide sequences,. The invention provides novel means for inhibiting undesirable OX40R-OX40L interactions and cell signaling associated to human diseases, which are of therapeutic and diagnostic importance.

L23 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2003:697001 Document No. 139:212907 Use of BCMA as an immunotherapeutic agent. Kalled, Susan L.; Reid, Hugh (Biogen, Inc., USA). PCT Int. Appl. WO 2003072713 A2 20030904, 72 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US5147 20030221. PRIORITY: US 2002-PV358427 20020221.

AB The disclosure relates to B-cell maturation antigen (BCMA), a receptor for APRIL and BAFF, and its use as an immunoregulatory agent in treatment of immunol. disorders such as multiple sclerosis. The disclosure provides methods and compns. for treating neurodegenerative immunol. disorders in mammals by administering soluble BCMA, an antibody against BCMA, or an antibody against a BCMA ligand, e.g., APRIL or BAFF. The soluble BCMA comprises the extracellular domain of BCMA fused to an Fc region of human IgG. BCMA-Fc therapy reduces the titer of CNS-specific autoantibodies and induces an anti-inflammatory Th2 cell switch.

L23 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2003:656809 Document No. 139:196279 **Chimeric proteins** comprising autoantigen epitope and effector molecule epitope for preventing and treating **autoimmune** diseases. Zocher, Marcel; Dreier, Torsten; Baeuerle, Patrick (Micromet A.-G., Germany). PCT Int. Appl. WO 2003068822 A2 20030821, 141 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP1389 20030212. PRIORITY: EP 2002-3332 20020213.

AB The present invention relates to a (poly)peptide construct consisting of at least two domains of at least two pluralities of domains wherein one of said domains or pluralities of domains comprises a de-immunized autoreactive antigen or (a) fragment(s) thereof specifically recognized by the Ig receptors of an autoreactive B-cells and wherein a/the further domain or plurality of domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes. Preferably, said (poly)peptide construct consisting of at least two domains comprises a de-immunized autoreactive antigen or (a) fragment which is MOG or (a) fragment(s) thereof and a second domain comprising an effector mol. is an anti-CD3 receptor or an Fc-part of an Ig. The invention also relates to compns. comprising the compds. of the invention. Described is also the use of the afore-mentioned (poly)peptide construct and further compds. for the preparation of a pharmaceutical composition for the treatment and/or prevention of an **autoimmune** disease. In addition, the present invention relates to method for treating, ameliorating and/or preventing of an **autoimmune** disease. Thus, MOG-CD3, MOG-Fc, mutated MOG-Fc and AchR-**Fc fusion** proteins were prepared for eliminating

autoreactive B cells.

L23 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2003:5348 Document No. 138:71922 Human interleukin 17-homologous polypeptides and polynucleotides and their therapeutic uses. Chen, Jian; Filvaroff, Ellen; Fong, Sherman; Goddard, Audrey; Godowski, Paul; Grimaldi, Christopher; Gurney, Austin; Li, Hanzhong; Hillan, Kenneth; Tumas, Daniel; Vanlookeren, Menno; Vandlen, Richard; Watanabe, Colin; Williams, P. Mickey; Wood, William I.; Yansura, Daniel (Genentech, Inc., USA). U.S. Pat. Appl. Publ. US 2003003546 A1 20030102, 129 pp., Cont.-in-part of U. S. Ser. No. 311,832. (English). CODEN: USXXCO. APPLICATION: US 2001-816744 20010322. PRIORITY: US 98-PV85579; 19980515; US 98-PV113621; 19981223; WO 99-US5028; 19990308; US 99-PV130232; 19990421; US 99-PV131022; 19990426; US 99-311832; 19990514; US 99-PV134287; 19990514; WO 99-US10733; 19990514; US 99-PV138387; 19990609; US 99-PV172096; 19991223; WO 99-US31274; 19991230; US 2000-PV175481; 20000111; WO 2000-US4341; 20000218; WO 2000-US5601; 20000301; WO 2000-US5841; 20000302; US 2000-PV191007; 20000321; WO 2000-US7532; 20000321; WO 2000-US15264; 20000602; US 2000-PV213807; 20000622; WO 2000-US23328; 20000824.

AB The present invention is directed to 9 novel human polypeptides having sequence similarity with interleukin 17 (IL-17), IL-17 receptors, and to nucleic acid mols. encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Further provided herein are methods for treating degenerative cartilaginous disorders and other inflammatory diseases.

L23 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2003:605872 Document No. 140:223006 Targeting and Blocking B7 Costimulatory Molecules on Antigen-Presenting Cells Using CTLA4Ig-Conjugated Liposomes: In Vitro Characterization and in Vivo Factors Affecting Biodistribution. Park, Chung-Gyu; Thiex, Natalie W.; Lee, Kyung-Mi; Szot, Gregory L.; Bluestone, Jeffery A.; Lee, Kyung-Dall (College of Pharmacy, Department of Pharmaceutical Sciences, University of Michigan, Ann Arbor, MI, 48109-1065, USA). Pharmaceutical Research, 20(8), 1239-1248 (English) 2003. CODEN: PHREEB. ISSN: 0724-8741. Publisher: Kluwer Academic/Plenum Publishers.

AB CTLA4Ig, a fusion protein of CTLA-4 and Fc of Ig (Ig) heavy chain, inhibits the essential costimulatory signal for full T cell activation via blocking the interaction between CD28 and B7 mols. and renders T cell nonresponsiveness. CTLA4Ig has been used to control deleterious T cell activation in many exptl. systems. We hypothesized that by conjugating CTLA4Ig to liposomes the efficacy of CTLA4Ig could be enhanced through multivalent ligand effect, superior targetability, and modification of the fate of ligated costimulatory mols. Consistent with this hypothesis, liposome-conjugated CTLA4Ig bound to B7 and blocked their binding sites more efficiently than free CTLA4Ig, lowering the half maximal dose for B7 blocking by an order of the magnitude. These results were similar both in B7-1 expressing p815 cells and in activated macrophages. Moreover, CTLA4Ig-liposomes underwent rapid internalization upon cell surface binding through B7 mols. In allogenic mixed lymphocyte reaction assays, the CTLA4Ig-liposomes were tested to show effective inhibition of T cell proliferation. In vivo, however, when CTLA4Ig-liposomes were injected into mice, a significant fraction was localized to the reticuloendothelial system (RES), presumably because of its binding to Fc receptors expressed on tissue macrophages. The Fc receptor-mediated uptake could be alleviated by coinjection of anti-FcR monoclonal antibody. In the mouse engrafted with pancreatic islets of Langerhans underneath the capsule of one kidney, despite the increased localization in RES, enhanced accumulation of CTLA4Ig-conjugated liposome was observed in the engrafted kidney compared to the contralateral kidney. Thus, the conjugation of

CTLA4Ig to liposome could increase the efficiency of the targeting by increasing the binding avidity at cellular level and by increasing the concentration at the target site in in vivo system. The biodistribution and circulation time data suggested that the CTLA4Ig-liposomes could be improved upon minimizing the FcR-mediated uptake by Fc receptor-bearing cells. Thus, the strategy of conjugating CTLA4Ig to liposomes could be exploited for immune intervention in transplantation and **autoimmune** diseases for the efficient blocking of costimulation.

L23 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2003:534925 Document No. 139:148329 Electro-gene therapy of collagen-induced arthritis by using an expression plasmid for the soluble p75 tumor necrosis factor receptor-**Fc fusion** protein. Kim, J.-M.; Ho, S.-H.; Hahn, W.; Jeong, J.-G.; Park, E.-J.; Lee, H.-J.; Yu, S. S.; Lee, C-S.; Lee, Y.-W.; Kim, S. (ViroMed Co., Ltd., Seoul, S. Korea). Gene Therapy, 10(15), 1216-1224 (English) 2003. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Nature Publishing Group.

AB Tumor necrosis factor (TNF) is a proinflammatory cytokine involved in the pathogenesis of rheumatoid arthritis, and antagonism of TNF may reduce the activity of the disease. Among a number of techniques for gene transfer in vivo, the direct injection of plasmid DNA into muscle is simple, inexpensive, and safe. In this study, we attempted to treat collagen-induced arthritis (CIA) with anti-TNF gene therapy by transferring the plasmid encoding soluble p75 TNF receptor linked to the Fc portion of human IgG1 (sTNFR:Fc) using in vivo electroporation. DBA/1 mice were immunized with bovine type II collagen and boosted with the same antigen. At 2 days after boosting, the plasmid vector containing cDNA for the sTNFR:Fc was injected into one selected site in the gastrocnemius muscle followed by electroporation. Serum levels of sTNFR:Fc reached 2.3 ng/mL on day 5 when gene expression reached its peak. Macroscopic anal. of paws for redness, swelling and deformities showed that the onset of moderate-to-severe CIA in mice treated with sTNFR:Fc was prevented on a significant level compared with the control mice ($P<0.05$). The beneficial effect of sTNFR:Fc DNA transfer lasted for at least 18 days following treatment. In addition, both the synovitis and the erosion of cartilage in the knee joints were dramatically reduced in mice treated with sTNFR:Fc ($P<0.05$). The expression of IL-1β and IL-12 in the paw was also decreased by sTNFR:Fc treatment ($P<0.01$) while there was little change in the levels of IL-17 and vWF. These data showed that sTNFR:Fc expression plasmid was effective in the prevention of CIA, and in vivo electroporation-mediated gene transfer may provide a new approach to cytokine therapy in **autoimmune** arthritis.

L23 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:967696 Document No. 138:203385 Gene therapy with plasmids encoding cytokine- or cytokine receptor-IgG **chimeric proteins.** Piccirillo, Ciriaco A.; Prud'homme, Gerald J. (Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA). Methods in Molecular Biology (Totowa, NJ, United States), 215(Cytokines and Colony Stimulating Factors), 153-170 (English) 2003. CODEN: MMBIED. ISSN: 1064-3745. Publisher: Humana Press Inc..

AB The methods for the delivery of vectors encoding cytokines and cytokine receptors for the prevention of treatment of **autoimmune** diseases are presented. The methods composed of plasmid DNA vector construction and expression, construction of interferon (IFN)-γR/IgG1 expression vector, transfection of COS-7 cells, IFN-γR/IgG1- **Fc fusion** protein ELISA assays, plasmid DNA preparation, i.m. injection of plasmid DNA, electroporation, extraction of luciferase from skeletal muscles, luciferase assays, lymphocyte proliferation and effector function, determination of plasma tumor-growth factor-β1 levels, polymerase chain reaction (PCR) and reverse transcription-PCR anal.

L23 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:927623 Document No. 138:21187 Human and murine attractin/mahogany-like polypeptides and their encoding polynucleotides and antibodies and methods of use. Anderson, Dirk M. (Immunex Corporation, USA). PCT Int. Appl. WO 2002097120 A1 20021205, 89 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US16391 20020523. PRIORITY: US 2001-PV293608 20010525; US 2001-PV324626 20010924.

AB The present disclosure provides human and murine cDNA sequences encoding homologs of attractin and mahogany (HAM) polypeptides and fragments thereof. Attractin is a human glycoprotein belonging to a family of proteins called the CUB family of cell adhesion and guidance proteins, and mahogony is the murine ortholog of human attractin. The open reading frame of human HAM is predicted to be encoded on 29 exons on human chromosome 10q26. Four putative alternatively spliced variants are found during PCR amplifications including a deletion of exon 7, deletion of exon 10, deletion of exon 19, and a deletion of exon 21; various single nucleotide polymorphisms are also identified. HAM possesses an extracellular region located at about amino acids 61 to 1230 of the precursor protein, as well as EGF-like domains, CUB domain, C-type lectin or carbohydrate-recognition domain (CLECT domain), KELCH motif, laminin EGF-like domain, and transmembrane and cytoplasmic domains. Tissue expression profiles indicate that HAM may be used as a tissue-specific marker. The invention also provides processes for production of recombinant forms of such polypeptides, antibodies generated against these polypeptides or fragments, and assays and methods employing these polypeptides, antibodies, and polynucleotides.

L23 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:927265 Document No. 138:20515 Human sialic acid-binding immunoglobulin-like lectin family member Siglec-12, its cloning and mapping and tissue expression, and related therapeutic use. Anderson, Dirk M.; Marken, John S. (Immunex Corporation, USA). PCT Int. Appl. WO 2002096452 A1 20021205, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US16906 20020529. PRIORITY: US 2001-PV294199 20010529.

AB Provided herein are polypeptide and polynucleotide sequences for a mol. having homol. to the siglec (sialic acid-binding Ig-like lectin) family of polypeptides. In particular, Siglec-12 is identified by sequence homolog search in genomic sequences of chromosome 19 (GenBank AC011452). The Siglec-12 gene (GenBank AF337818 referenced, in fact it corresponds to Siglec-11) has 11 exons and 10 introns and is mapped on chromosome 19q13.4, approx. 1.2-1.3 megabases distal to Siglec-5. Siglec-12 comprises predicted signal peptide (amino acid position: 1-14), five Ig domains (14-141, 142-235, 253-340, 357-443, and 444-538), a transmembrane domain (550-570), a cytoplasmic domain (571-686, with two signaling motifs at 630-635 and 654-659), and a number of conserved cysteine residues. The Siglec-12 mRNA tissue expression profile is also provided. Also provided are methods of making and using a siglec-like polypeptide and polynucleotide, and using these recombinant Siglec-12 for the treatment of related diseases.

L23 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:315096 Document No. 136:320419 Human IL-17-related protein LP-48 and therapeutic use thereof. Glasebrook, Andrew Lawrence; Liu, Ling; Newton, Christy Michelle; Tetreault, Jonathan Wendell (Eli Lilly and Company, USA). PCT Int. Appl. WO 2002033083 A2 20020425, 112 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US27737 20010928. PRIORITY: US 2000-PV240177 20001013; US 2001-PV309936 20010803.

AB The invention provides protein and cDNA sequences for a novel human IL-17-related protein called LP-48 (also known as IL-17C and IL-21), which is a member of interleukin superfamily. The transgenic mice expressing LP-48 are used to test the function of LP-48 and possible therapeutic applications. LP-48 can protect the transgenic mice against LPS-induced septic shock and from LPS-induced death. LP-48 protein can inhibit LPS-induced increases in IFN-γ, IL-12, TNF-α and IL-6 secretion in transgenic mice. LP-48 can reduce apoptosis in human endothelial cells, more specifically, apoptosis induced by staurosporine. LP-48 can bind to the cell surface of endothelial cells and other tissues specifically through natural LP-48 receptors. Methods are provided for the treatment or prevention of atherosclerosis, allergic **autoimmune** diseases, endothelial cell apoptosis, allograft vasculopathy, hypertension, congestive heart failure, ischemia/reperfusion injury, type 1 diabetes, inflammation, immunodeficiencies, cancers, and infectious diseases by administering a human IL-17 related polypeptide and/or an antibody recognizing an epitope thereof to a patient in need of such therapy.

L23 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:429403 Document No. 137:2752 Monoclonal antibodies for the detection of decoy receptor 3-assocd. disease, hybridomas producing said antibodies and DcR3-IgG1 **Fc fusion** proteins for therapy. Mai, Shen-Chih; Liu, Shih-Jen (Taiwan). U.S. Pat. Appl. Publ. US 2002068064 A1 20020606, 12 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-998196 20011203. PRIORITY: TW 2000-89125856 20001205.

AB The invention provides monoclonal antibodies against decoy receptor 3 (DcR3), hybridomas producing said antibodies, kits containing said monoclonal antibodies and uses of the hybridomas, antibodies and kits for the detection of DcR3-associated diseases, as well as for the treatment and/or prevention of DcR3-associated diseases. The use of fusion proteins consisting of DcR3 and IgG1 Fc fragment for treatment and prevention of DcR3-associated diseases is also discussed.

L23 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2002:409195 Document No. 137:1567 Human apoptosis inducing molecule II and its cDNA and use thereof in drug screening and therapy. Ebner, Reinhard; Yu, Guo-liang; Ruben, Steven M.; Ullrich, Stephen (Human Genome Sciences, Inc., USA). U.S. Pat. Appl. Publ. US 2002064869 A1 20020530, 79 pp., Cont.-in-part of U.S. Ser. No. 822,953, abandoned. (English). CODEN: USXXCO. APPLICATION: US 1998-27287 19980220. PRIORITY: US 1996-PV13923 19960322; US 1996-PV30157 19961031; US 1997-822953 19970321.

AB The present invention relates to a novel member of the TNF-Ligand superfamily, Apoptosis Inducing Mol. II (AIM II). In particular, isolated nucleic acid mols. are provided encoding the human AIM II protein. AIM II polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The effect of AIM II on the cell growth are tested in breast cancer cell line or xenograft human breast carcinoma cell MDA in nude mice. Soluble AIM II can mediate cytotoxicity in HT-29 cell and stimulate secretion of IFNγ in human PBL cells. Cell surface expression of β-lymphokine receptor fusion protein LTβR-Fc or

TR2-**Fc fusion** protein can block soluble AIM II-mediated cytotoxicity in HT-29 cells and AIM II can bind to LTβR specifically. The invention further relates to screening methods for identifying agonists and antagonists of AIM II activity. Also provided are therapeutic methods for treating lymphadenopathy, **autoimmune** disease, graft vs. host disease, and to inhibit neoplasia, such as tumor cell growth.

L23 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2002:183343 Document No. 136:308120 A single-chain class II MHC-IgG3 fusion protein inhibits **autoimmune** arthritis by induction of antigen-specific hyporesponsiveness. Zuo, Li; Cullen, Constance M.; DeLay, Monica L.; Thornton, Sherry; Myers, Linda K.; Rosloniec, Edward F.; Boivin, Gregory P.; Hirsch, Raphael (Division of Rheumatology, Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, 45229, USA). Journal of Immunology, 168(5), 2554-2559 (English) 2002. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB T cells play a central role in many **autoimmune** diseases. A method to specifically target the function of autoreactive T cell clones would avoid the global immunosuppression associated with current therapies. To develop a mol. capable of inhibiting autoreactive T cell responses in vivo, single-chain peptide-I-A-IgG3 fusion proteins were constructed and expressed in both mammalian and insect cells. The fusion proteins were designed with an IgG3 Fc moiety to make them divalent, allowing TCR crosslinking, while lacking FcR binding and costimulation. The fusion proteins stimulated T cell hybridomas in vitro in a peptide-specific, MHC-restricted manner but failed to do so in soluble form. In vivo administration of an I-Aq fusion protein, containing an immunodominant collagen II peptide, significantly delayed the onset and reduced the severity of collagen-induced arthritis in DBA/1 mice by induction of Ag-specific hyporesponsiveness. Such fusion proteins may be useful to study novel therapeutic approaches for T cell-mediated **autoimmune** diseases.

L23 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2002:268259 Document No. 137:4864 Blockade of T cell Costimulatory Signals using Adenovirus Vectors Prevents both the Induction and the Progression of Experimental **Autoimmune** Myocarditis. Matsui, Yutaka; Inobe, Manabu; Okamoto, Hiroshi; Chiba, Satoru; Shimizu, Toshihiro; Kitabatake, Akira; Uede, Toshimitsu (Division of Molecular Immunology, Institute for Genetic Medicine, Hokkaido University, Sapporo, 060-0815, Japan). Journal of Molecular and Cellular Cardiology, 34(3), 279-295 (English) 2002. CODEN: JMCDAY. ISSN: 0022-2828. Publisher: Academic Press.

AB Exptl. **autoimmune** myocarditis (EAM) has been used as a model for human myocarditis in relation to the **autoimmune** mechanism and proved to be a T cell-mediated **autoimmune** disease. Interactions of T cell surface receptors CD28 and CD40L with their ligands B7 and CD40, resp., on APCs are critical for antigen-specific T cell activation under physiol. and pathol. conditions. To achieve effective inhibition of these interactions, we have constructed adenovirus vectors containing CTLA4Ig (AdexCTLA4Ig) and CD40Ig (AdexCD40Ig) and examined the effects of these adenovirus vectors in preventing EAM. AdexLacZ as a control, or AdexCTLA4Ig and/or AdexCD40Ig were injected i.v. into rats on day 0 or 14 after immunization to study the preventive effects on EAM in the T cell activation phase or inflammatory phase. Disease severity was estimated by the macroscopic and microscopic findings of the heart, heart weight to body weight ratios, and cellular and humoral immune responses on day 21. The onset of EAM after AdexCTLA4Ig or AdexCD40Ig treatment on day 0 was completely inhibited and antigen-specific lymphocyte proliferation was significantly reduced in those adenovirus-treatment groups, suggesting that those therapies induce antigen-specific T cell anergy. Moreover, significant reduction in disease severity was achieved after the adenovirus vector treatment even on day 14 compared with EAM rats. This study indicates the therapeutic potential of costimulatory pathway blockade by gene-transfer

in myocarditis. (c) 2002 Academic Press.

L23 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2001:904738 Document No. 136:36346 Soluble CD1 antigens. Gumperz, Jenny E.; Brenner, Michael B.; Behar, Samuel M. (The Brigham and Women's Hospital, Inc., USA). PCT Int. Appl. WO 2001094949 A2 20011213, 88 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18178 20010605. PRIORITY: US 2000-PV209416 20000605.
AB The authors disclose the preparation and characterization of CD1 fusion proteins. In one example, a soluble CD1d antigen was shown to present α-galactosylceramide to CD1-restricted T-cells. In a second example, the recognition of tumor phospholipids by CD1-restricted T-cells was demonstrated.

L23 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2001:816912 Document No. 135:356771 Preparation and modulatory activity of human anti-CD40 antibodies. Mikayama, Toshifumi; Takahashi, Nobuaki; Chen, Xingjie; Schoenberger, Stephen P. (Gemini Science, Inc., USA). PCT Int. Appl. WO 2001083755 A2 20011108, 60 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13672 20010427. PRIORITY: US 2000-PV200601 20000428.
AB The authors disclose the preparation and characterization of human antibodies that bind CD40. Using a CD40-Fc immunogen, the authors immunized human Ig locus-transgenic mice and generated antibody-secreting hybridomas using standard methodol. In one example, a human anti-CD40 antibody was shown to enhance B-cell proliferative responses to CD40 ligand. In a second example, human anti-CD40 antibodies were shown to up-regulate CD95 expression on Ramos cells.

L23 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2001:798070 Document No. 135:343299 Bispecific opsonins. Himawan, Jeff (Elusys Therapeutics, Inc., USA). PCT Int. Appl. WO 2001080883 A1 20011101, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13161 20010424. PRIORITY: US 2000-PV199903 20000426; US 2000-PV244812 20001101.
AB The author discloses bispecific mols. that are characterized by having a first domain which binds an antigen and a second domain which binds the C3b-like receptor (known as complement receptor 1 (CR1) or CD35 in primates). In one example, a bispecific antibody is prepared that targets both IgE and the C3b receptor.

L23 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and methods of therapeutic use. Ware, Carl F. (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.

AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric soluble forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-β receptor (LTβR). The present invention is also based upon the discovery that HVEM polypeptides have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-**Fc fusion** proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, **autoimmune** diseases, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

L23 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2001:507485 Document No. 135:91544 PP14 fusion proteins and methods for making and using the same. Tykocinski, Mark L.; Riely, Gregory J. (TR Associates, L.L.C., USA). PCT Int. Appl. WO 2001049163 A1 20010712, 28 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US104 20010103. PRIORITY: US 2000-PV174287 20000103.

AB Novel fusion proteins comprising PP14 are disclosed. The fusion proteins retain the immunoregulatory function of native PP14, but offer significant advantages. Methods for using the fusion proteins, and sequence encoding the same, in the treatment of immune system diseases and disorders are therefore also disclosed, as are methods for recombinant production of the present fusion proteins. The fusion proteins comprise PP14 and Ig Fc regions.

L23 ANSWER 25 OF 28 MEDLINE on STN

2001269555. PubMed ID: 11244034. Anti-TNF alpha therapy of rheumatoid arthritis: what have we learned?. Feldmann M; Maini R N. (Kennedy Institute of Rheumatology Division, Imperial College School of Medicine, 1 Aspenlea Road, London W6 8LH, United Kingdom.. m.feldmann@ic.ac.uk) . Annual review of immunology, (2001) 19 163-96. Ref: 160. Journal code: 8309206. ISSN: 0732-0582. Pub. country: United States. Language: English.

AB Rheumatoid arthritis (RA), a systemic disease, is characterized by a chronic inflammatory reaction in the synovium of joints and is associated with degeneration of cartilage and erosion of juxta-articular bone. Many pro-inflammatory cytokines including TNF alpha, chemokines, and growth factors are expressed in diseased joints. The rationale that TNF alpha played a central role in regulating these molecules, and their pathophysiological potential, was initially provided by the demonstration that anti-TNF alpha antibodies added to in vitro cultures of a representative population of cells derived from diseased joints inhibited the spontaneous production of IL-1 and other pro-inflammatory cytokines. Systemic administration of anti-TNF alpha antibody or sTNFR fusion protein

to mouse models of RA was shown to be anti-inflammatory and joint protective. Clinical investigations in which the activity of TNF alpha in RA patients was blocked with intravenously administered infliximab, a chimeric anti-TNF alpha monoclonal antibody (mAB), has provided evidence that TNF regulates IL-6, IL-8, MCP-1, and VEGF production, recruitment of immune and inflammatory cells into joints, angiogenesis, and reduction of blood levels of matrix metalloproteinases-1 and -3. Randomized, placebo-controlled, multi-center clinical trials of human TNF alpha inhibitors have demonstrated their consistent and remarkable efficacy in controlling signs and symptoms, with a favorable safety profile, in approximately two thirds of patients for up to 2 years, and their ability to retard joint damage. Infliximab (a mAB), and etanercept (a sTNF-R-**Fc fusion** protein) have been approved by regulatory authorities in the United States and Europe for treating RA, and they represent a significant new addition to available therapeutic options.

L23 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

2000:491303 Document No. 133:206649 Treatment of murine lupus with cDNA encoding IFN-γR/Fc. Lawson, Brian R.; Prud'homme, Gerald J.; Chang, Yigang; Gardner, Humphrey A.; Kuan, Jason; Kono, Dwight H.; Theofilopoulos, Argyrios N. (Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA). Journal of Clinical Investigation, 106(2), 207-215 (English) 2000. CODEN: JCINAO. ISSN: 0021-9738. Publisher: American Society for Clinical Investigation.

AB IFN-γ, a pleiotropic cytokine, is a key effector mol. in the pathogenesis of several **autoimmune** diseases, including lupus. Importantly, deletion of IFN-γ or IFN-γR in several lupus-predisposed mouse strains resulted in significant disease reduction, suggesting the potential for therapeutic intervention. We evaluated whether i.m. injections of plasmids with cDNA encoding IFN-γR/Fc can retard lupus development and progression in MRL-Faslpr mice. Therapy significantly reduced serum levels of IFN-γ, as well as disease manifestations (autoantibodies, lymphoid hyperplasia, glomerulonephritis, mortality), when treatment was initiated at the predisease stage, particularly when IFN-γR/Fc expression was enhanced by electroporation at the injection site. Remarkably, disease was arrested and even ameliorated when this treatment was initiated at an advanced stage. This therapy represents a rare example of disease reversal and makes application of this nonviral gene therapy in humans with lupus (and perhaps other **autoimmune**/inflammatory conditions) highly promising.

L23 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

1999:635456 Document No. 131:270947 Recombinant soluble CD40 ligand polypeptide and pharmaceutical composition containing the same. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K.; Srinivasan, Subhashini; Gibson, Marylou G.; Morris, Arvia E.; McGrew, Jeffrey T. (Immunex Corporation, USA). U.S. US 5962406 A 19991005, 64 pp., Cont.-in-part of U.S. Ser. No. 249,189. (English). CODEN: USXXAM. APPLICATION: US 1995-484624 19950607. PRIORITY: US 1991-783707 19911025; US 1991-805723 19911205; US 1992-969703 19921023; US 1994-249189 19940524.

AB Disclosed are polypeptides (e.g. membrane bound CD40-L, monomeric and oligomeric CD40-L, soluble CD40-L, and fusion protein of CD40-L) and antisense and sense DNA and RNA sequences, vectors and transformed host cells useful in providing CD40-L polypeptides. More particularly, this invention provides isolated human and murine CD40-L polypeptides that bind to the extracellular binding region of a CD40 receptor. Also, provided are soluble CD40 comprising extracellular region of human CD40 and CD40/**Fc fusion** proteins, and antibodies. CD40 agonists, i.e. membrane-bound CD40-L and oligomeric CD40-L, are useful as vaccine adjuvant and for stimulating B cell proliferation and monoclonal antibody production from hybridoma cells. CD40 antagonists, i.e. CD40 receptor, CD40/**Fc fusion** protein, soluble CD40/Fc, monomeric CD40-L, are useful for treating **autoimmune** diseases characterized by presence of high levels of antigen-antibody complexes, such as allergy,

insulin dependent diabetes mellitus, graft vs. host disease and others.

L23 ANSWER 28 OF 28 MEDLINE on STN
97272173. PubMed ID: 9127018. A noncytolytic IL-10/**Fc fusion** protein prevents diabetes, blocks autoimmunity, and promotes suppressor phenomena in NOD mice. Zheng X X; Steele A W; Hancock W W; Stevens A C; Nickerson P W; Roy-Chaudhury P; Tian Y; Strom T B. (Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA 02215, USA.) Journal of immunology (Baltimore, Md. : 1950), (1997 May 1) 158 (9) 4507-13. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB We have been successful in our efforts to develop a long lived noncytolytic murine IL-10/**Fc fusion** protein. In the nonobese diabetic mouse (NOD) model, administration of IL-10/Fc from 5 to 25 wk of age completely prevented the occurrence of diabetes. Moreover, these mice remained disease-free long after cessation of IL-10/Fc therapy. Immunohistochemistry studies show that IL-10/Fc treatment inhibits expression of TNF-alpha, proinflammatory cytokine, as well as Th1-type cytokines, IL-2 and IFN-gamma, but promotes expression of IL-4 and IL-10, Th2-type cytokines, by islet-infiltrating leukocytes. In an adoptive transfer model of diabetes in NOD mice, we found that: 1) IL-10/Fc treated hosts bear leukocytes that block expression of diabetes and 2) these leukocytes persisted even 8 wk after cessation of IL-10/Fc treatment. The potent antidiabetogenic effects provided by IL-10/Fc in the NOD model, together with its apparent lack of systemic toxicity, are notable.

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=> s "MBP-Fc"
L24           0 "MBP-FC"

=> s saxon a?/au
L25        1313 SAXON A?/AU

=> s l25 and Fc fusion
L26           8 L25 AND FC FUSION

=> dup remove l26
PROCESSING COMPLETED FOR L26
L27           2 DUP REMOVE L26 (6 DUPLICATES REMOVED)

=> d l27 1-2 cbib abs
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L27 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
2004433011. PubMed ID: 15316510. Inhibition of allergen-specific IgE reactivity by a human Ig Fcgamma-Fcepsilon bifunctional fusion protein. Zhang Ke; Kepley Christopher L; Terada Tetsuya; Zhu Daocheng; Perez Hector; **Saxon Andrew.** (Hart and Louis Lyon Laboratory, Division of Clinical Immunology and Allergy, Department of Medicine, University of California Los Angeles School of Medicine, CA 90095-1680, USA.) Journal of allergy and clinical immunology, (2004 Aug) 114 (2) 321-7. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: Coaggregating FcepsilonRI with FcgammaRII receptors holds great potential for treatment of IgE-mediated disease by inhibiting FcepsilonRI signaling. We have previously shown that an Fcgamma-Fcepsilon fusion protein, human IgG-IgE **Fc fusion** protein (GE2), could inhibit FcepsilonRI-mediated mediator releases in vitro and in vivo. OBJECTIVE: We sought to test whether GE2 was capable of blocking mediator release from FcepsilonRI cells sensitized with IgE in vivo or in vitro before exposure to GE2, a critical feature for GE2 to be clinically applicable. METHODS: GE2 was tested for its ability to inhibit Fel d 1-induced mediator release from human blood basophils from subjects with cat allergy, human lung-derived mast cells, human FcepsilonRIalpha transgenic mice sensitized with human cat allergic serum, and rhesus monkeys naturally allergic to the dust mite Dermatophagoides farinae.

RESULTS: Basophils from subjects with cat allergy and lung mast cells degranulate when challenged with Fel d 1 and anti-IgE, respectively. GE2 itself did not induce mediator release but strongly blocked this Fel d 1- and anti-IgE-driven mediator release. GE2 was able to block Fel d 1-driven passive cutaneous anaphylaxis at skin sites sensitized with human serum from subjects with cat allergy in human FcepsilonRIalpha transgenic mice, but by itself, GE2 did not induce a passive cutaneous anaphylaxis reaction. Finally, GE2 markedly inhibited skin test reactivity to D farinae in monkeys naturally allergic to this allergen, with complete inhibition being observed at 125 ng. CONCLUSION: GE2 is able to successfully compete for FcepsilonRs and FcgammaRs on cells presensitized in vitro and in vivo and lead to inhibition of IgE-mediated reactivity through coaggregation of FcepsilonRI with FcgammaRII.

L27 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2
94267214. PubMed ID: 7515920. CD58 (LFA-3) stimulation provides a signal for human isotype switching and IgE production distinct from CD40. Diaz-Sanchez D; Chegini S; Zhang K; **Saxon A.** (Hart and Louise Lyon Laboratory, Department of Medicine, UCLA School of Medicine 90024-1680.) Journal of immunology (Baltimore, Md. : 1950), (1994 Jul 1) 153 (1) 10-20. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Induction of an IgE response involves several discrete steps: 1) induction of epsilon germ line transcription, 2) DNA recombination, and 3) mature RNA transcription/translation. Here we show that ligation of B cell CD58 by CD2, its natural ligand on T cells, or by mAb, provides a novel IL-4-dependent signal for the latter two steps. Highly purified human B cells were induced to produce IgE by costimulation with IL-4 and CD58 mAb. Although CD58 ligation alone was unable to induce epsilon germ-line transcription, in concert with IL-4-stimulated epsilon germ-line transcription it induced the appearance of productive epsilon transcripts and IgE production. The direct involvement of CD2 was demonstrated: B cells cultured with IL-4 plus murine T hybridoma cells transfected with human CD2 produced IgE. A CD40 **Fc fusion** protein had no effect on CD58-driven IgE production while inhibiting CD40-dependent responses. Furthermore, cells from patients with common variable immunodeficiency produced IgE in response to IL-4 plus CD40 mAb but not to IL-4 plus CD58 mAb. CD58-driven IgE synthesis was IFN-gamma independent and was not enhanced by exogenous IL-6. Functional differences between CD40 and CD58 IgE stimulation were demonstrated. Thus, the CD2:CD58 ligand/counterligand system provides an alternative pathway by which cell contact signaling may regulate IgE. Given the relative importance of CD2 triggering on mucosal T cells and the mucosal location of IgE production, this may be especially true on mucosal surfaces.

```
=> s l25 and IgE
L28         388 L25 AND IGE

=> dup remove l28
PROCESSING COMPLETED FOR L28
L29          166 DUP REMOVE L28 (222 DUPLICATES REMOVED)

=> s l29 and IgE Fc
L30            7 L29 AND IGE FC

=> dup remove l30
PROCESSING COMPLETED FOR L30
L31            7 DUP REMOVE L30 (0 DUPLICATES REMOVED)

=> d l31 1-7 cbib abs
```

L31 ANSWER 1 OF 7 MEDLINE on STN
2004433011. PubMed ID: 15316510. Inhibition of allergen-specific **IgE** reactivity by a human Ig Fcgamma-Fcepsilon bifunctional fusion

protein. Zhang Ke; Kepley Christopher L; Terada Tetsuya; Zhu Daocheng; Perez Hector; **Saxon Andrew.** (Hart and Louis Lyon Laboratory, Division of Clinical Immunology and Allergy, Department of Medicine, University of California Los Angeles School of Medicine, CA 90095-1680, USA.) Journal of allergy and clinical immunology, (2004 Aug) 114 (2) 321-7. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Coaggregating FcepsilonRI with FcgammaRII receptors holds great potential for treatment of **IgE**-mediated disease by inhibiting FcepsilonRI signaling. We have previously shown that an Fcgamma-Fcepsilon fusion protein, human IgG-**IgE Fc** fusion protein (GE2), could inhibit FcepsilonRI-mediated mediator releases in vitro and in vivo. OBJECTIVE: We sought to test whether GE2 was capable of blocking mediator release from FcepsilonRI cells sensitized with **IgE** in vivo or in vitro before exposure to GE2, a critical feature for GE2 to be clinically applicable. METHODS: GE2 was tested for its ability to inhibit Fel d 1-induced mediator release from human blood basophils from subjects with cat allergy, human lung-derived mast cells, human FcepsilonRIalpha transgenic mice sensitized with human cat allergic serum, and rhesus monkeys naturally allergic to the dust mite Dermatophagoides farinae. RESULTS: Basophils from subjects with cat allergy and lung mast cells degranulate when challenged with Fel d 1 and anti-**IgE**, respectively. GE2 itself did not induce mediator release but strongly blocked this Fel d 1- and anti-**IgE**-driven mediator release. GE2 was able to block Fel d 1-driven passive cutaneous anaphylaxis at skin sites sensitized with human serum from subjects with cat allergy in human FcepsilonRIalpha transgenic mice, but by itself, GE2 did not induce a passive cutaneous anaphylaxis reaction. Finally, GE2 markedly inhibited skin test reactivity to D farinae in monkeys naturally allergic to this allergen, with complete inhibition being observed at 125 ng. CONCLUSION: GE2 is able to successfully compete for FcepsilonRs and FcgammaRs on cells presensitized in vitro and in vivo and lead to inhibition of **IgE**-mediated reactivity through coaggregation of FcepsilonRI with FcgammaRII.

L31 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. **Saxon, Andrew** (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-847208 20010501.

AB The invention concerns bifunctional fusion mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., **IgE** -mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L31 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and **IgE** receptor-binding epitope for treating allergies and other immune diseases. **Saxon, Andrew**; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp.

DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-847208 20010501; US 2001-439 20011024.

AB The invention concerns bifunctional fusion mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., **IgE** -mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L31 ANSWER 4 OF 7 MEDLINE on STN

89093929. PubMed ID: 2521348. Binding the low affinity Fc epsilon R on B cells suppresses ongoing human **IgE** synthesis. Sherr E; Macy E; Kimata H; Gilly M; **Saxon A.** (Department of Medicine, UCLA School of Medicine, Los Angeles, CA 90024.) Journal of immunology (Baltimore, Md. : 1950), (1989 Jan 15) 142 (2) 481-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Our results support the hypothesis that binding the low affinity Fc epsilon R (Fc epsilon R-II, CD23) on **IgE**-secreting B cells, directly suppresses **IgE** production. **IgE** production from AF-10/U266 (a human **IgE** plasmacytoma) decreased upon incubation with anti-**IgE** mAb or **IgE**:anti-**IgE** immune complexes (**IgE**-IC). Synthesis was suppressed a maximum of 51% with 10 micrograms/ml of **IgE**-IC after a 24-h incubation. Spontaneous in vitro **IgE** synthesis from the B cells of highly atopic individuals was also inhibited in a similar fashion. This effect was isotype specific as IgA or IgG immune complexes did not alter **IgE** production from AF-10 nor did **IgE**-IC affect IgA or IgG synthesis from lymphoblastoid cell lines making IgG (GM1500 and RPMI 8866) or IgA (GM1056). U266/AF-10 cells displayed both membrane **IgE** (greater than 90%) and Fc epsilon R-II (23%). To evaluate the role of these membrane proteins in the observed suppression of **IgE** synthesis, we treated U266/AF-10 cells with **IgE**-IC that bound Fc epsilon R-II but could not bind membrane **IgE**, as the mAb used was directed against an idiotypic determinant on the myeloma **IgE** (PS) used to make the **IgE**-IC. Suppression was maximal (greater than 50%) with these complexes at 0.1 micrograms/ml and at a 1/1 ratio of mAb anti-**IgE** to human myeloma **IgE.** When **IgE** -IC were used that were constructed with heat denatured **IgE** or F(ab')2 fragments of **IgE**, suppression was abrogated indicating **IgE-Fc** epsilon R binding was required. Neither PS **IgE** nor mAb 5.1 (the components of **IgE**-IC) alone affected **IgE** synthesis. Furthermore, a mAb binding directly to CD23 suppressed **IgE** synthesis from AF-10 up to 60%. Using limiting dilution analysis, we determined that **IgE** production per AF-10 cell was constant (0.9 pg/cell/24 h), independent of cell density and cells incubated with **IgE**-IC were uniformly suppressed. To clarify the mechanism of **IgE**-IC-induced

suppression on AF-10 cells, we assessed both the proliferative rate and cell cycle distribution upon incubation with **IgE**-IC. There was no correlation between **IgE** production and [3H]TdR incorporation by AF-10 cells incubated with **IgE**-IC or anti-CD23 mAb. The distribution of cells within the cell cycle was unaffected by these treatments, with 60% of the cells in G1. These results define a direct role for the Fc epsilon R-II on B cells in the regulation of ongoing **IgE** synthesis.

L31 ANSWER 5 OF 7 MEDLINE on STN

88270763. PubMed ID: 2968873. Expression of Fc epsilon receptors and surface and cytoplasmic **IgE** on human fetal and adult lymphopoietic tissue. Kanowith-Klein S; Hofman F; **Saxon A.** (Department of Medicine, UCLA, Los Angeles, California 90024.) Clinical immunology and immunopathology, (1988 Aug) 48 (2) 214-24. Journal code: 0356637. ISSN: 0090-1229. Pub. country: United States. Language: English.

AB The appearance during ontogeny of **IgE**-positive and Fc epsilon receptor (FcER)-bearing cells was studied. Monoclonal antibody to the constant region (Fc) of **IgE** (CIA-E-7.12) was used to detect cytoplasmic and surface **IgE.** A monoclonal antibody to the low-affinity Fc epsilon receptor (FcER-II = CD23) and immune complexes composed of human **IgE** and mouse monoclonal anti-human **IgE Fc** were used to detect FcER. Cryostat sections of human fetal tissues (liver, lung, spleen, and thymus) from 11 to 22 weeks gestation as well as adult tonsil tissues were examined for **IgE**, FcER, and other lymphoid markers by immunoperoxidase staining. Although both **IgE**- and FcER-positive cells were present in adult tissues, we found that, in contrast to an earlier report, such cells were not present in the fetal tissues examined. The in situ location of FcER on cells in human lymphoid tissues revealed that the FcER-bearing cells were localized predominantly in the germinal centers (mature B cell and macrophage areas) of the tonsil follicles with some staining in the mantle (resting and less mature B cell areas).

L31 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

1987:154462 Document No. 106:154462 Natural killer cell interaction with **IgE** in the control of ongoing human **IgE** synthesis. Kimata, Hajime; **Saxon, Andrew** (Sch. Med., UCLA, Los Angeles, CA, 90024, USA). International Archives of Allergy and Applied Immunology, 82(4), 419-21 (English) 1987. CODEN: IAAAAM. ISSN: 0020-5915.

AB Fresh natural killer (NK) cells from normal donors inhibited **IgE** synthesis from U266/AF-10 cells via a direct cytolytic effect. This inhibition was reversed by incubation of NK cells with human **IgE** -anti-**IgE** immune complexes (**IgE**-IC) for 16 h without a decrease in NK-mediated cytotoxicity. Upon incubation with **IgE** -IC, **IgE Fc** receptors (FcER) were induced on 3-9% of NK cells. These **IgE**-IC induced FcER+ NK cells from normal donors secreted (an) **IgE**-specific factor(s) which enhanced U266/AF-10 **IgE** production without increasing DNA synthesis. Production of this **IgE** differentiation factor(s) explains the apparent reversal of NK cell inhibition of **IgE** production

L31 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

1987:136649 Document No. 106:136649 A mechanism for the suppression of ongoing **IgE** synthesis. Sherr, Elliott H.; **Saxon, Andrew** (Dep. Med., UCLA, Los Angeles, CA, 90024, USA). International Archives of Allergy and Applied Immunology, 82(4), 414-16 (English) 1987. CODEN: IAAAAM. ISSN: 0020-5915.

AB **IgE** synthesis from the human plasmacytoma U266/AF-10 was suppressed by addition of **IgE** immune complexes (**IgE**-IC). This suppression was isotype-specific as synthesis from other B cell lines was unaffected. Using **IgE**-IC constructed with a monoclonal antibody that recognizes PS protein-**IgE** and not ND **IgE** (the **IgE** protein made by U266/AF-10), it was shown that this suppression was mediated through the crosslinking of the Fcε